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(75) 発明者/出願人 (米国についてのみ): 日沼 州司 (HINUMA, Shuji) [JP/JP]; 〒305-0821 茨城県 つくば市 春日 1 丁目 7 番地 9 武田春日ハイツ 1402 号 Ibaraki (JP). 藤井 亮 (FUJII, Ryo) [JP/JP]; 〒305-0821 茨城県 つくば市 春日 2 丁目 33 番地 16 Ibaraki (JP). 大儀 和宏 (OGI, Kazuhiro) [JP/JP]; 〒305-0045 茨城県 つくば市 梅園 2 丁目 16 番 1 号 ルンビーニ梅園 206 号 Ibaraki (JP). 小松 秀俊 (KOMATSU, Hidetoshi) [JP/JP]; 〒305-0821 茨城県 つくば市 春日 1 丁目 7 番地 9 武田春日ハイツ 803 号 Ibaraki (JP). 川俣 裕二 (KAWAMATA, Yuji) [JP/JP]; 〒305-0035 茨城県 つくば市 松代 4 丁目 22 番地 松代 4 丁目団地 2 号棟 203 号 Ibaraki (JP). 細谷 昌樹 (HOSOYA, Masaki) [JP/JP]; 〒300-0007 茨城県 土浦市 板谷 1 丁目 711 番地の 83 Ibaraki (JP).
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- (71) 出願人 (米国を除く全ての指定国について): 武田薬品工業株式会社 (TAKEDA CHEMICAL INDUSTRIES, LTD.) [JP/JP]; 〒541-0045 大阪府 大阪市 中央区道修町四丁目 1 番 1 号 Osaka (JP).
- (74) 代理人: 小林 浩, 外 (KOBAYASHI, Hiroshi et al.); 〒104-0028 東京都 中央区 八重洲 2 丁目 8 番 7 号 福岡ビル 9 階 Tokyo (JP).

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(54) Title: METHOD OF DETERMINING LIGAND

(54) 発明の名称: リガンドの決定方法



(57) Abstract: It is intended to provide a method of determining a ligand to an orphan receptor. More specifically speaking, it is intended to provide a method of a ligand to a receptor protein, to which no ligand has been determined, characterized by using a fused protein of the receptor protein with a fluorescent protein.

(57) 要約:

本発明は、オーファンレセプターのリガンドの決定方法の提供を目的とする。

具体的には、本発明はリガンドが決定されていないレセプタータンパク質と蛍光タンパク質との融合タンパク質を用いることを特徴とする該レセプタータンパク質に対するリガンドの決定方法等を提供する。

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## 1

## 明細書

## リガンドの決定方法

## 技術分野

- 5 本発明は、細胞膜に存在するレセプタータンパク質に対するリガンドの決定方法、特にリガンドが全く未知である、いわゆるオーファンレセプターのリガンドの決定方法に関する。

## 背景技術

- 10 多くのホルモンや神経伝達物質などの生理活性物質は、細胞膜に存在する特異的なレセプタータンパク質を通じて生体の機能を調節している。これらのレセプタータンパク質のうち多くは共役しているguanine nucleotide-binding protein (以下、Gタンパク質と略称する)の活性化を通じて細胞内のシグナル伝達を行ない、また、7個の膜貫通領域を有する共通した構造をもっていることから、G
- 15 タンパク質共役型レセプタータンパク質あるいは7回膜貫通型レセプタータンパク質(7TMR)と総称される。

Gタンパク質共役型レセプタータンパク質は生体の細胞や臓器の各機能細胞表面に存在し、それら細胞や臓器の機能を調節する分子、例えば、ホルモン、神経伝達物質および生理活性物質等の標的として生理的に重要な役割を担っている。

- 20 レセプターは生理活性物質との結合を介してシグナルを細胞内に伝達し、このシグナルにより細胞の賦活や抑制といった種々の反応が惹起される。

- 各種生体の細胞や臓器の機能を調節する物質と、その特異的なレセプタータンパク質、特にGタンパク質共役型レセプタータンパク質との関係を明らかにすることは、各種生体の細胞や臓器の機能を解明し、それら機能と密接に関連した医薬品開発に非常に重要な手段を提供することとなる。
- 25

従来、Gタンパク質共役型レセプタータンパク質と生理活性物質(すなわち、リガンド)との結合を阻害する物質や、結合して生理活性物質(すなわち、リガンド)と同様なシグナル伝達を引き起こす物質は、これらレセプターの特異的なアンタゴニストまたはアゴニストとして、生体機能を調節する医薬品として活用

されてきた。

しかし、現時点でもなお、対応するリガンドが同定されていない、いわゆるオーファンレセプターが多数存在しており、そのリガンドの決定および機能解明が切望されている。

- 5     Gタンパク質共役型レセプターのシグナル伝達作用を指標とする、新たな生理活性物質（すなわち、リガンド）の探索、また、該レセプターに対するアゴニストまたはアンタゴニストの探索は有用である。これら該レセプターに対するリガンド、アゴニストまたはアンタゴニストなどは、Gタンパク質共役型レセプターの機能不全に関連する疾患の予防および／または治療薬や診断薬として活用することが期待できる。

GFP (Green Fluorescent Protein) は中生動物のオワンクラゲに由来する発光タンパク質の一種である (WO 96/23810、WO 96/27675、WO 97/26333、WO 97/28261、WO 97/42320)。

- 15     Multiple レスポンスエレメント (MRE) および cAMP レスポンスエレメント (CRE) とレポーター活性とを組み合わせ、Gi、Gs または Gq 共役型オーファン受容体のリガンドを決定する方法が報告されている (Analytical Biochemistry, 275, 54-61, 1999)。

- 20     cAMP レスポンスエレメント (CRE) とレポーター活性とを組み合わせ、Gs または Gq 共役型オーファン受容体と相互作用する分子をスクリーニングする方法が報告されている (Analytical Biochemistry, 226, 349-354, 1995)。

- 25     cAMP レスポンスエレメント (CRE) とレポーター活性とを組み合わせ、リガンドが知られている Gi または Gs 共役型受容体の特徴を調べる方法が報告されている (Current Opinion in Biotechnology, 1995, 6: 574-581)。

Gタンパク質共役型レセプターとの共役関係の曖昧さを増大させたキメラGタンパク質αサブユニット、キメラGタンパク質を発現させた細胞を用いてGタンパク質共役型レセプターの反応を検出する方法が報告されている (WO 01/36481)



組換え型酵母発現ライブラリーを用いたオーファンG蛋白質共役型レセプターのリガンドの同定方法が報告されている (US P 6, 255, 059)。

- 5 受容体と試験ペプチドの両方を含有する細胞からなり、オーファン受容体の同定あるいはスクリーニングに有用な細胞の受容体活性修飾物質の同定方法が報告されている (US 2001/0026926)。

オーファン受容体のリガンドを同定するための *Saccharomyces* 有性生殖系を利用した発現システムが報告されている (WO 00/031261)。

- 10 従来のリガンドの探索・決定方法では、例えば真核生物由来の細胞を用いて、リガンドをスクリーニングする場合、該レセプターを安定的に発現する、いわゆる安定細胞株 (stable cell line) を樹立しなければならず、この細胞株の樹立には特別な細胞を必要とした。またスクリーニングには複数の測定の組合せが必要であり、試験化合物が複数存在すると、時間がかかるためにその実施が困難であった。つまり、従来のリガンド等の探索・決定方法には、(1) 使用可能な細胞系が限定される、(2) 該細胞系の樹立に時間がかかる、(3) 複数の測定法を組み合わせるために、検体数が多くなるとその実施が困難になる等の問題があった。これらの問題を解決するための、各種の細胞系が使用でき、かつ短時間で実施できるリガンドの決定方法が望まれている。
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#### 発明の開示

- 本発明者らは、鋭意研究を重ねた結果、リガンドが決定されていないレセプタータンパク質と GFP 等の蛍光タンパク質との融合タンパク質を安定的にあるいは一過性に発現させた細胞を作製することにより、GFP 等の蛍光タンパク質の
- 25 蛍光または GFP 抗体等の蛍光タンパク質抗体を利用した免疫染色法やウエスタンブロット法など用いて、

(1) タンパク質レベルでレセプタータンパク質が発現していることを確認でき

(2) 細胞膜にレセプタータンパク質が発現していることを確認でき、

- (3) レセプタータンパク質の発現量を見積もることができ、  
(4) レセプタータンパク質の高発現細胞を選択でき、そして  
(5) リガンドによるレセプターの特異的反応を、レセプターと蛍光タンパク質との融合タンパク質の細胞内へのインターナリゼーションとして検出できること  
5 等を見出し、これらの特徴を利用することにより、リガンドが決定されていないレセプタータンパク質（以下、オーファンレセプターと略記する場合がある）のリガンドを効率よく決定できることを見出した。本発明者らは、これらの知見に基づいて、さらに研究を重ねた結果、本発明を完成するに至った。

すなわち、本発明は、

- 10 [1] リガンドが決定されていないレセプタータンパク質と蛍光タンパク質との融合タンパク質を用いることを特徴とする該レセプタータンパク質に対するリガンドの決定方法、  
[2] リガンドが決定されていないレセプタータンパク質とGFPとの融合タンパク質を用いることを特徴とする上記[1]記載のリガンドの決定方法、  
15 [3] リガンドが決定されていないレセプタータンパク質とGFPとの融合タンパク質を発現している細胞またはその細胞膜面分と、試験化合物とを接触させることを特徴とする上記[1]記載のリガンドの決定方法、  
[4] (1) アラキドン酸遊離、アセチルコリン遊離、細胞内 $Ca^{2+}$ 遊離、細胞内cAMP生成、細胞内cGMP生成、イノシトールリン酸産生、細胞膜電位  
20 変動、細胞内タンパク質のリン酸化、c-fos活性化またはpHの低下を促進する活性または抑制する活性、(2) MAPキナーゼの活性化、(3) 転写因子の活性化、(4) ジアシルグリセロール産生、(5) 細胞膜上のイオンチャネルの開閉、(6) アポトーシスの誘導、(7) 形態変化、(8) 該融合タンパク質の細胞膜から細胞質への移行、(9) 低分子量Gタンパク質の活性化、(10)  
25 ) 細胞分裂促進活性または(11) DNA合成促進活性を測定することを特徴とする上記[1]記載のリガンドの決定方法、  
[5] 該融合タンパク質の細胞膜から細胞質への移行を測定することを特徴とする上記[1]記載のリガンドの決定方法、  
[6] GFP蛍光を観察することにより該融合タンパク質の細胞膜から細胞質へ

の移行を測定する上記〔5〕記載のリガンドの決定方法、

〔7〕リガンドが決定されていないレセプタータンパク質と蛍光タンパク質との融合タンパク質を発現し、かつ、cAMPレスポンスエレメント／プロモーターの下流にレポータータンパク質をコードするDNAを連結したプラスミドを含有する細胞と試験化合物とを接触させて、レポータータンパク質の活性を測定することを特徴とする上記〔1〕記載のリガンドの決定方法、

〔8〕（1）リガンドが決定されていないレセプタータンパク質と蛍光タンパク質との融合タンパク質をコードするDNAを含有するプラスミドおよび（2）cAMPレスポンスエレメント／プロモーターの下流にレポータータンパク質をコードするDNAを連結したプラスミドを含有する細胞を培養し、試験化合物と接触させてレポータータンパク質の活性を測定することを特徴とする上記〔7〕記載の方法、

〔9〕リガンドが決定されていないレセプタータンパク質とGFPとの融合タンパク質を発現し、かつ、cAMPレスポンスエレメント／プロモーターの下流にレポータータンパク質をコードするDNAを連結したプラスミドを含有する細胞と試験化合物とを接触させて、レポータータンパク質の活性を測定することを特徴とする上記〔2〕記載のリガンドの決定方法、

〔10〕（1）リガンドが決定されていないレセプタータンパク質とGFPとの融合タンパク質をコードするDNAを含有するプラスミドおよび（2）cAMPレスポンスエレメント／プロモーターの下流にレポータータンパク質をコードするDNAを連結したプラスミドを含有する細胞を培養し、試験化合物と接触させてレポータータンパク質の活性を測定することを特徴とする上記〔9〕記載の方法、

〔11〕レセプタータンパク質がGタンパク質共役型レセプタータンパク質である上記〔1〕記載の方法、

〔12〕GFPが配列番号：1、配列番号：3、配列番号：5または配列番号：7で表わされるアミノ酸配列と同一または実質的に同一のアミノ酸配列を含有するタンパク質である上記〔1〕記載の方法、

〔13〕プロモーターがTATA様配列である上記〔7〕記載の方法、

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- [14] レポータータンパク質がルシフェラーゼである上記[7]記載の方法、  
[15] プラスミドがcAMPレスポンスエレメントの下流にTATA様プロモーターおよびレポータータンパク質をコードする遺伝子を連結したものである上記[7]記載の方法、
- 5 [16] 細胞が、リガンドが決定されていない2種類以上のレセプタータンパク質を発現している上記[7]記載の方法、  
[17] 細胞が、抑制性Gタンパク質 $\alpha$ サブユニットGiをコードする遺伝子を含有するプラスミドを更に含有する上記[7]記載の方法、  
[18] さらにフォルスコリンを添加する上記[7]記載の方法、
- 10 [19] 2種類以上のレセプタータンパク質が類似の特徴を有することを特徴とする上記[16]記載の方法、  
[20] 類似の特徴がレポータータンパク質の基礎発現量および（または）フォルスコリン添加時のレポータータンパク質の発現量である上記[19]記載の方法、
- 15 [21] 予め2種類以上のレセプタータンパク質をそれぞれ単独で発現させた時のレポータータンパク質の基礎発現量および／またはフォルスコリン添加時のレポータータンパク質の発現量を測定し、該レポータータンパク質の発現量が同程度である2種類以上のレセプタータンパク質を組み合わせ発現させることを特徴とする上記[16]記載の方法、
- 20 [22] リガンドが決定されていないレセプタータンパク質と蛍光タンパク質との融合タンパク質またはその塩、  
[23] 蛍光タンパク質がGFPである上記[22]記載の融合タンパク質またはその塩、  
[24] 上記[22]記載の融合タンパク質をコードするDNAを含有するDNA、
- 25 A、  
[25] 上記[22]記載のDNAを含有する組換えベクター、  
[26] 上記[25]記載の組換えベクターで形質転換させた形質転換体、  
[27] リガンドが決定されていないレセプタータンパク質に対するリガンドを決定するための蛍光タンパク質の使用、

[28] リガンドが決定されていないレセプタータンパク質に対するリガンドを決定するためのGFPの使用に関する。

#### 図面の簡単な説明

- 5 図1は、TGR5発現ベクターを導入したHEK293細胞(A)および元のベクターのみを導入したHEK293細胞(B)における、コレステロール代謝関連物質によるレポーター活性化の検出(n=2)の結果を示す。

図2は、HEK293細胞におけるリガンド刺激に対するレポーター遺伝子の発現誘導の結果を示す。

- 10 図3は、Gi共存下でのTGR5のリトコール酸に対する反応の結果を示す。

図4は、リガンド非存在下における、CHO細胞に発現させたTGR5-GFP融合タンパク質の局在を示す。図中の白線は4μmを示す。

図5は、TGR5-GFPを発現させたCHO細胞にTLCAを添加して30分後の融合タンパク質の局在を示す。図中の白線は4μmを示す。

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#### 発明を実施するための最良の形態

本発明のリガンド決定方法は、(1) リガンドが決定されていないレセプタータンパク質と蛍光タンパク質との融合タンパク質を用いることを特徴とする方法であり、具体的には、リガンドが決定されていないレセプタータンパク質と蛍光

20 タンパク質との融合タンパク質を発現している細胞またはその細胞膜画分と、試験化合物とを接触させることを特徴とする方法である(リガンド決定方法A)。

- さらには、本発明のリガンドの決定方法は、(1) リガンドが決定されていないレセプタータンパク質と蛍光タンパク質との融合タンパク質を発現し、かつエンハンサー/プロモーターの下流にレポータータンパク質をコードするDNAを連結したプラスミドを含有する細胞と試験化合物とを接触させて、発現誘導され
- 25 るレポータータンパク質の活性を測定する方法、(2) (i) リガンドが決定されていないレセプタータンパク質と蛍光タンパク質との融合タンパク質をコードするDNAを含有するプラスミドおよび(ii) エンハンサー/プロモーターの下流にレポータータンパク質をコードするDNAを連結したプラスミドを含有す

る細胞を培養し、試験化合物と接触させて、発現誘導されるレポータータンパク質の活性を測定する方法である（以上、リガンド決定法B）。

本発明に用いられるオーファンレセプターとしては、例えばGタンパク質共役型レセプタータンパク質などが用いられる。具体例としては、配列番号：9で表わされるアミノ酸配列と同一もしくは実質的に同一のアミノ酸配列を含有するGタンパク質共役型レセプタータンパク質や、WO 96/05302、EP-A-711831、EP-A-789076、EP-A-1103563、EP-A-1103562、特開平8-154682号公報、特開平8-283295号公報、特開平8-196278号公報、特開平8-245697号公報、特開平8-266280号公報、特開平9-51795号公報、特開平9-121865号公報、特開平9-2388686号公報、特開平10-146192号公報に記載のGタンパク質共役型レセプタータンパク質などが挙げられる。

蛍光タンパク質としては、視覚によって認識し得るタンパク質であれば特に限定されることはなく、例えば、GFP (Green Fluorescent Protein)、Tag配列、EGFP (enhanced greenfluorescent protein)、ECFP (enhanced cyan fluorescent protein)、EYFP (Enhanced yellow fluorescent protein)、DsRED (Discosoma sp. Red Fluorescent Protein)、EBFP (Enhanced blue fluorescent protein) などが用いられる。

GFPは、中生動物のオワンクラゲに由来する発光タンパク質の一種であり、配列番号：1、配列番号：3、配列番号：5または配列番号：7で表わされるアミノ酸配列と同一もしくは実質的に同一のアミノ酸配列を含有するタンパク質などである。

配列番号：1、配列番号：3、配列番号：5または配列番号：7で表わされるアミノ酸配列と実質的に同一のアミノ酸配列としては、例えば、配列番号：1、配列番号：3、配列番号：5または配列番号：7で表わされるアミノ酸配列と約70%以上、好ましくは約80%以上、さらに好ましくは約90%以上、最も好ましくは約95%以上の相同性を有するアミノ酸配列などが挙げられる。

本発明の配列番号：1、配列番号：3、配列番号：5または配列番号：7で表わされるアミノ酸配列と実質的に同一のアミノ酸配列を含有するタンパク質とし

ては、例えば、配列番号：1、配列番号：3、配列番号：5または配列番号：7で表わされるアミノ酸配列と実質的に同一のアミノ酸配列を有し、かつ配列番号：1、配列番号：3、配列番号：5または配列番号：7で表わされるアミノ酸配列からなるタンパク質と実質的に同質の活性を有するタンパク質などが好ましい

5 .

GFPの活性としては、例えば、励起光照射による発光などが挙げられる。実質的に同質の活性とは、それらの活性が性質的に同質であることを示す。したがって、それらの活性が同等（例、約0.01～100倍、好ましくは約0.5～20倍、より好ましくは約0.5～2倍）であることが好ましいが、活性の程度

10 やタンパク質の分子量などの量的要素は異なってもよい。

GFPにおける励起光照射による発光などの活性の測定は、公知の方法に準じて行なうことができる。

また、GFPとしては、(1) 配列番号：1、配列番号：3、配列番号：5または配列番号：7で表わされるアミノ酸配列中の1または2個以上（好ましくは、1～30個程度、より好ましくは1～10個程度、さらに好ましくは数個（1～5個））のアミノ酸が欠失したアミノ酸配列、(2) 配列番号：1、配列番号：3、配列番号：5または配列番号：7で表わされるアミノ酸配列に1または2個以上（好ましくは、1～30個程度、より好ましくは1～10個程度、さらに好ましくは数個（1～5個））のアミノ酸が付加または挿入したアミノ酸配列、

15 (3) 配列番号：1、配列番号：3、配列番号：5または配列番号：7で表わされるアミノ酸配列中の1または2個以上（好ましくは、1～30個程度、より好ましくは1～10個程度、さらに好ましくは数個（1～5個））のアミノ酸が他のアミノ酸で置換されたアミノ酸配列、または(4) それらの欠失・付加・置換を組み合わせたアミノ酸配列を含有するタンパク質なども用いられ、なかでも（

20 i) 配列番号：1、配列番号：3、配列番号：5または配列番号：7で表わされるアミノ酸配列のN末端のメチオニン残基が欠失しているアミノ酸配列または（

25 ii) 配列番号：1で表わされるアミノ酸配列のN末端のメチオニン残基が欠失し、さらに次のアラニン残基がスレオニン残基またはセリン残基に置換されたアミノ酸配列を含有するタンパク質などが好ましく用いられる。

- 具体的には、例えば、(i) 配列番号：1、配列番号：3、配列番号：5または配列番号：7で表わされるアミノ酸配列からなるGFP、(ii) 配列番号：1、配列番号：3、配列番号：5または配列番号：7で表わされるアミノ酸配列のN末端のメチオニン残基が欠失しているアミノ酸配列からなるGFP、(iii)
- 5 配列番号：1で表わされるアミノ酸配列のN末端のメチオニン残基が欠失し、さらに次のアラニン残基がスレオニン残基またはセリン残基に置換されたアミノ酸配列からなるGFPなどが用いられる。

Tag配列としては、例えば、以下の公知配列が用いられる。

- (1) His-tag (PCDNA3.1/His A)
- 10 His His His His His His (配列番号：17)
- (2) V5-tag (PCDNA3.1/V5-His A)
- Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser Thr (配列番号：18)
- )
- (3) myc-tag (pCDNA3.1/myc-His A)
- 15 Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu (配列番号：19)
- (4) Xpress-tag (PCDNA3.1/His A)
- Asp Leu Tyr Asp Asp Asp Asp Lys (配列番号：20)
- (5) HA-tag (PcluzHA Expression vector)
- Met Gly Ser Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Ser Leu Glu Phe (配列番号：21)
- 20

EGFPとしては、配列番号：7で表わされるアミノ酸配列からなるタンパク質が用いられる。

ECFPとしては、配列番号：22で表わされるアミノ酸配列からなるタンパク質が用いられる。

- 25 EYFPとしては、配列番号：24で表わされるアミノ酸配列からなるタンパク質が用いられる。

DsREDとしては、配列番号：26で表わされるアミノ酸配列からなるタンパク質が用いられる。

EBFPとしては、配列番号：28で表わされるアミノ酸配列からなるタンパ



ク質が用いられる。

これらEGFP、ECFP、EYFP、DsRED、EBFPは、励起光照射による発光などの活性を有する限り、（１）上記したアミノ酸配列中の１または２個以上（好ましくは、１～３０個程度、より好ましくは１～１０個程度、さらに好ましくは数個（１～５個））のアミノ酸が欠失したアミノ酸配列、（２）上記したアミノ酸配列に１または２個以上（好ましくは、１～３０個程度、より好ましくは１～１０個程度、さらに好ましくは数個（１～５個））のアミノ酸が付加または挿入しているアミノ酸配列、（３）上記したアミノ酸配列中の１または２個以上（好ましくは、１～３０個程度、より好ましくは１～１０個程度、さらに好ましくは数個（１～５個））のアミノ酸が他のアミノ酸で置換されているアミノ酸配列、または（４）それらの欠失・付加・置換を組み合わせたアミノ酸配列を有するタンパク質であってもよい。

GFPをコードするDNAとしては、具体的には、例えば、配列番号：２、配列番号：４、配列番号：６または配列番号：８で表される塩基配列を含有するDNA、または配列番号：２、配列番号：４、配列番号：６または配列番号：８で表わされる塩基配列の相補的塩基配列とハイストリンジェントな条件下でハイブリダイズする塩基配列を有し、かつ配列番号：１、配列番号：３、配列番号：５または配列番号：７で表されるアミノ酸配列からなるGFPと実質的に同質の活性（例、励起光照射による発光など）を有するタンパク質をコードするDNAであれば何れのものでよい。

配列番号：２、配列番号：４、配列番号：６または配列番号：８で表わされる塩基配列とハイブリダイズできるDNAとしては、例えば、配列番号：２、配列番号：４、配列番号：６または配列番号：８で表わされる塩基配列と約７０％以上、好ましくは約８０％以上、より好ましくは約９０％以上、最も好ましくは約９５％以上の相同性を有する塩基配列を含有するDNAなどが用いられる。

ハイブリダイゼーションは、公知の方法あるいはそれに準じる方法、例えば、モレキュラー・クローニング（Molecular Cloning）2nd（J. Sambrook et al., Cold Spring Harbor Lab. Press, 1989）に記載の方法などに従って行なうことができる。また、市販のハイブリダイゼーション用試薬を使用する場合、添付の

使用説明書に記載の方法に従って行なうことができる。より好ましくは、ハイス  
トリンジエントな条件に従って行なうことができる。

該ハイストリンジエントな条件とは、例えば、ナトリウム濃度が約 19～40  
mM、好ましくは約 19～20 mMで、温度が約 50～70℃、好ましくは約 6  
5 0～65℃の条件を示す。特に、ナトリウム濃度が約 19 mMで温度が約 65℃  
の場合が最も好ましい。

より具体的には、配列番号：1で表わされるアミノ酸配列からなる GFP をコ  
ードする DNA は、配列番号：2で表わされる塩基配列を含有する DNA (WO  
97/42320) などであり、配列番号：3で表わされるアミノ酸配列からな  
る GFP をコードする DNA は、配列番号：4で表わされる塩基配列を含有する  
10 DNA (WO 96/23810) などであり、配列番号：5で表わされるアミノ  
酸配列からなる GFP (GFPuv) をコードする DNA は、配列番号：6で表  
わされる塩基配列を含有する DNA (WO 97/26333) などであり、配列  
番号：7で表わされるアミノ酸配列からなる GFP (EGFP) をコードする D  
15 NA は、配列番号：8で表わされる塩基配列を含有する DNA (NCBI Accessio  
n No. AAB0572) などである。

配列番号：7で表わされるアミノ酸配列からなる EGFP をコードする DNA  
としては、配列番号：8で表わされる塩基配列からなる DNA などが用いられる  
。

20 配列番号：22で表わされるアミノ酸配列からなる ECFP をコードする DNA  
としては、配列番号：23で表わされる塩基配列からなる DNA などが用いられ  
る。

配列番号：24で表わされるアミノ酸配列からなる EYFP をコードする DNA  
としては、配列番号：25で表わされる塩基配列からなる DNA などが用いられ  
25 る。

配列番号：26で表わされるアミノ酸配列からなる DsRED をコードする DN  
A としては、配列番号：27で表わされる塩基配列からなる DNA などが用いら  
れる。

配列番号：28で表わされるアミノ酸配列からなる EBFp をコードする DN

Aとしては、配列番号：29で表わされる塩基配列からなるDNAなどが用いられる。

オーファンレセプターと蛍光タンパク質との融合タンパク質は、オーファンレセプタータンパク質をコードするDNAとGFPをコードするDNAとを連結したDNAを用いて製造することができる。

該連結DNAは、オーファンレセプターをコードするDNAの塩基配列の3'末端に、インフレームでGFPをコードするDNAの5'末端を連結して構築する。

なお、両DNAの間にAla、Gly、Serなど分子量の小さいアミノ酸残基から選ばれる1～5個程度のリンカーと呼ばれるアミノ酸配列をコードするDNAを挿入してもよい。

オーファンレセプターと蛍光タンパク質との融合タンパク質（以下、融合タンパク質と略記する場合がある）の発現ベクターは、例えば、（1）融合タンパク質をコードするDNA断片を調製し、（2）該DNA断片を適当な発現ベクター中のプロモーターの下流に連結することにより製造することができる。

リガンドが決定されていないレセプタータンパク質と蛍光タンパク質との融合タンパク質としては、例えば、配列番号：30～配列番号：131のいずれかの配列番号で表されるアミノ酸配列からなる、リガンドが決定されていない102種類の各レセプタータンパク質と配列番号：1で表されるアミノ酸配列からなるGFPとの融合タンパク質が好ましく用いられる。これら配列番号：30～配列番号：131のいずれかの配列番号で表されるアミノ酸配列においては、配列番号：1で表されるアミノ酸配列のN末端のメチオニン残基が欠失しており、場合によっては、さらに次のアラニン残基がスレオニン残基またはセリン残基に置換されている。

この融合タンパク質をコードするDNAは、リガンドが決定されていない102種類の各レセプタータンパク質をコードする部分の下流に、配列番号：1で表されるアミノ酸配列からなるGFPをコードするDNA（配列番号：2）を連結することによって調製でき、具体的には配列番号132～配列番号：233のいずれかの配列番号で表される塩基配列からなるDNAが用いられる。これら配列

番号：132～配列番号：233のいずれかの配列番号で表される塩基配列においては、配列番号：2で表される塩基配列の5'末端のメチオニン残基コドンが欠失しており、場合によっては、さらに次のアラニン残基コドンがスレオニン残基コドンまたはセリン残基コドンに置換されている。

- 5 発現ベクターとしては、大腸菌由来のプラスミド（例、pCR4、pCR2.1、pBR322、pBR325、pUC12、pUC13）、枯草菌由来のプラスミド（例、pUB110、pTP5、pC194）、酵母由来プラスミド（例、pSH19、pSH15）、 $\lambda$ ファージなどのバクテリオファージ、レトロウイルス、ワクシニアウイルス、バキュロウイルスなどの動物ウイルスなどの他、
- 10 pA1-11、pXT1、pRc/CMV、pRc/RSV、pcDNA1/Neoなどが用いられる。

- 該ベクターで用いられるプロモーターは、遺伝子発現に用いる宿主内で機能する適切なプロモーターであればいかなるものでもよい。例えば、動物細胞を宿主として用いる場合は、SR $\alpha$ プロモーター、SV40プロモーター、LTRプロモーター、CMVプロモーター、HSV-TKプロモーターなどが用いられる。
- 15 これらのうち、CMVプロモーター、SR $\alpha$ プロモーターなどが好ましい。

- また、各種組織において発現させる場合、インスリンII・プロモーター（膵臓）、Glycoprotein- $\alpha$ サブユニット・プロモーター（下垂体）、トランスサイレチン・プロモーター（肝臓）、レニン・プロモーター（腎臓）、
- 20 PSE・プロモーター（前立腺）、CD2・プロモーター（T細胞）、IgG-heavy chain・プロモーター（B細胞）、スカベンジャーレセプターA・プロモーター（マクロファージ）などが用いられる。

- 宿主がエシェリヒア属菌である場合は、trpプロモーター、lacプロモーター、recAプロモーター、 $\lambda$ P<sub>L</sub>プロモーター、lppプロモーターなどが
- 25 、宿主がバチルス属菌である場合は、SPO1プロモーター、SPO2プロモーター、penPプロモーターなど、宿主が酵母である場合は、PHO5プロモーター、PGKプロモーター、GAPプロモーター、ADHプロモーターなどが好ましい。宿主が昆虫細胞である場合は、ポリヘドリンプロモーター、P10プロモーターなどが好ましい。

該発現ベクターは、以上の他に、所望によりエンハンサー、スプライシングシグナル、ポリA付加シグナル、選択マーカー、SV40複製オリジン（以下、SV40oriと略称する場合がある）などを含有しうる。選択マーカーとして、例えば、ジヒドロ葉酸還元酵素（以下、dhfrと略称する場合がある）遺伝子

5 [メソトレキセート（MTX）耐性]、アンピシリン耐性遺伝子（以下、Amp<sup>r</sup>と略称する場合がある）、ネオマイシン耐性遺伝子（以下、Neo<sup>r</sup>と略称する場合がある、G418耐性）等が挙げられる。特に、CHO（dhfr<sup>-</sup>）細胞を用いてdhfr遺伝子を選択マーカーとして使用する場合、目的遺伝子をチミジンを含まない培地によっても選択できる。

- 10 また、必要に応じて、宿主に合ったシグナル配列を、本発明のレセプタータンパク質のN末端側に付加する。宿主がエシェリヒア属菌である場合は、PhoA・シグナル配列、OmpA・シグナル配列などが、宿主がバチルス属菌である場合は、 $\alpha$ -アミラーゼ・シグナル配列、サブチリシン・シグナル配列などが、宿主が酵母である場合は、MF $\alpha$ ・シグナル配列、SUC2・シグナル配列など、
- 15 宿主が動物細胞である場合には、インシュリン・シグナル配列、 $\alpha$ -インターフェロン・シグナル配列、抗体分子・シグナル配列などがそれぞれ利用できる。

このようにして構築されたレセプタータンパク質と蛍光タンパク質との融合タンパク質をコードするDNAを含有する発現ベクターを用いて、形質転換体を製造することができる。

- 20 宿主としては、例えば、エシェリヒア属菌、バチルス属菌、酵母、昆虫細胞、昆虫、動物細胞などが用いられる。

エシェリヒア属菌の具体例としては、エシェリヒア・コリ（*Escherichia coli*）K12・DH1（Proc. Natl. Acad. Sci. USA, 60, 160 (1968)）、JM103（Nucleic Acids Research, 9, 309 (1981)）、JA221（Journal of Molecular Biology, 120, 517 (1978)）、HB101（Journal of Molecular Biology, 41, 459 (1969)）、C600（Genetics, 39, 440 (1954)）、DH5 $\alpha$ （Inoue, H., Nojima, H. and Okayama, H., Gene, 96, 23-28 (1990)）、DH10B（Proc. Natl. Acad. Sci. USA, 87, 4645-4649 (1990)）などが用いられる。

25

バチルス属菌としては、例えば、バチルス・ズブチルス（*Bacillus subtilis*

) M I 1 1 4 (Gene, 24, 255 (1983))、2 0 7-2 1 (Journal of Biochemistry, 95, 87 (1984)) などが用いられる。

酵母としては、例えば、サッカロマイセス・セレビスエ (*Saccharomyces cerevisiae*) A H 2 2, A H 2 2 R<sup>-</sup>, N A 8 7-1 1 A, D K D-5 D、2 0 B-  
5 1 2、シゾサッカロマイセス・ポンベ (*Schizosaccharomyces pombe*) N C Y C  
1 9 1 3, N C Y C 2 0 3 6、ピキア・パストリス (*Pichia pastoris*) などが  
用いられる。

昆虫細胞としては、例えば、ウイルスが A c N P V の場合は、ヨトウガの幼虫  
由来株化細胞 (*Spodoptera frugiperda* cell; S f 細胞)、*Trichoplusia ni* の  
10 中腸由来の M G 1 細胞、*Trichoplusia ni* の卵由来の High Five<sup>TM</sup> 細胞、*Mamestra*  
*brassicae* 由来の細胞または *Estigmena acrea* 由来の細胞などが用いられる。ウ  
イルスが B m N P V の場合は、カイコ由来株化細胞 (*Bombyx mori* N; B m N 細  
胞) などが用いられる。該 S f 細胞としては、例えば、S f 9 細胞 (ATCC CRL17  
11)、S f 2 1 細胞 (以上、Vaughn, J. L. ら、In Vivo, 13, 213-217 (1977))  
15 などが用いられる。

昆虫としては、例えば、カイコの幼虫などが用いられる〔前田ら、Nature, 31  
5, 592 (1985)〕。

動物細胞としては、例えば、サル細胞 C O S-7, V e r o, チャイニーズハ  
ムスター細胞 C H O (以下、C H O 細胞と略記)、d h f r 遺伝子欠損チャイニ  
20 ーズhamster細胞 C H O (以下、C H O (d h f r<sup>-</sup>) 細胞と略記)、マウス  
L 細胞、マウス A t T-2 0、マウスミエローマ細胞、ラット G H 3、ヒト F L  
細胞、脾臓由来細胞 (R I N m 5 F, H I T-T 1 5 など)、下垂体由来細胞 (G H 3, G H 1, R C 4/B C など)、胎盤由来細胞 (B e W o, J A R, J E  
G-3 など)、肝臓由来細胞 (H e p G 2 など)、腎臓由来細胞 (A C H N など  
25 )、血球細胞由来細胞 (H 9, T H P-1, U-9 3 7 など)、H e L a 細胞な  
どが用いられる。

エシェリヒア属菌を形質転換するには、例えば、Proc. Natl. Acad. Sci. USA  
, 69, 2110 (1972) や、Gene, 17, 107 (1982) などに記載の方法に従って行なうこ  
とができる。

バチルス属菌を形質転換するには、例えば、Molecular & General Genetics, 168, 111 (1979)などに記載の方法に従って行なうことができる。

酵母を形質転換するには、例えば、Methods in Enzymology, 194, 182-187 (1991)、Proc. Natl. Acad. Sci. USA, 75, 1929 (1978)などに記載の方法に従っ

5 て行なうことができる。

昆虫細胞または昆虫を形質転換するには、例えば、Bio/Technology, 6, 47-55 (1988)などに記載の方法に従って行なうことができる。

動物細胞を形質転換するには、例えば、細胞工学別冊8新細胞工学実験プロト  
コール、263-267 (1995) (秀潤社発行)、Virology, 52, 456 (197

10 3)に記載の方法に従って行なうことができる。

このようにして、上記融合タンパク質をコードするDNAを含有する発現ベク  
ターで形質転換された形質転換体を得られる。

宿主がエシェリヒア属菌、バチルス属菌である形質転換体を培養する際、培養  
に使用される培地としては液体培地が適当であり、その中には該形質転換体の生  
15 育に必要な炭素源、窒素源、無機物その他が含有せしめられる。炭素源としては  
、例えば、グルコース、デキストリン、可溶性澱粉、ショ糖など、窒素源として  
は、例えば、アンモニウム塩類、硝酸塩類、コーンスチープ・リカー、ペプトン  
、カゼイン、肉エキス、大豆粕、バレイショ抽出液などの無機または有機物質、  
無機物としては、例えば、塩化カルシウム、リン酸二水素ナトリウム、塩化マグ  
20 ネシウムなどが挙げられる。また、酵母エキス、ビタミン類、生長促進因子など  
を添加してもよい。培地のpHは約5～8が望ましい。

エシェリヒア属菌を培養する際の培地としては、例えば、グルコース、カザミ  
ノ酸を含むM9培地〔ミラー (Miller)、Journal of Experiments in Molecula  
r Genetics, 431-433, Cold Spring Harbor Laboratory, New York (1972)〕が  
25 好ましい。ここに必要によりプロモーターを効率よく働かせるために、例えば、  
3β-インドリルアクリル酸のような薬剤を加えることができる。

宿主がエシェリヒア属菌の場合、培養は通常約15～43℃で約3～24時間  
行ない、必要により、通気や攪拌を加えることもできる。

宿主がバチルス属菌の場合、培養は通常約30～40℃で約6～24時間行な

い、必要により通気や攪拌を加えることもできる。

宿主が酵母である形質転換体を培養する際、培地としては、例えば、パークホルダー (Burkholder) 最小培地 [Bostian, K. L. ら、Proc. Natl. Acad. Sci. USA, 77, 4505 (1980)] や 0.5% カザミノ酸を含有する SD 培地 [Bitter, G. A. ら、Proc. Natl. Acad. Sci. USA, 81, 5330 (1984)] が挙げられる。培地の pH は約 5~8 に調整するのが好ましい。培養は通常約 20℃~35℃ で約 24~72 時間行ない、必要に応じて通気や攪拌を加える。

宿主が昆虫細胞または昆虫である形質転換体を培養する際、培地としては、Grace's Insect Medium (Grace, T. C. C., Nature, 195, 788 (1962)) に非働化した 10% ウシ血清等の添加物を適宜加えたものなどが用いられる。培地の pH は約 6.2~6.4 に調整するのが好ましい。培養は通常約 27℃ で約 3~5 日間行ない、必要に応じて通気や攪拌を加える。

宿主が動物細胞である形質転換体を培養する際、培地としては、例えば、約 5~20% の胎児牛血清を含む MEM 培地 [Science, 122, 501 (1952)]、DME M 培地 [Virology, 8, 396 (1959)]、RPMI 1640 培地 [The Journal of the American Medical Association, 199, 519 (1967)]、199 培地 [Proceeding of the Society for the Biological Medicine, 73, 1 (1950)] などが用いられる。pH は約 6~8 であるのが好ましい。培養は通常約 30℃~40℃ で約 15~60 時間行ない、必要に応じて通気や攪拌を加える。

各種宿主について適当な培地、培養条件などについては公知である（特に、WO 00/14227 号公報第 24 頁第 24 行~第 26 頁第 8 行、EP 1111047 A2 号公報段落 [0090]~[0096] 参照）。

以上のようにして、形質転換体の細胞膜に融合タンパク質を発現させることができる。

上記培養物から融合タンパク質を分離精製するには、例えば、下記の方法により行なうことができる。

融合タンパク質を培養菌体あるいは細胞から抽出するに際しては、培養後、公知の方法で菌体あるいは細胞を集め、これを適当な緩衝液に懸濁し、超音波、リゾチームおよび/または凍結融解などによって菌体あるいは細胞を破壊したのち



、遠心分離やろ過により融合タンパク質の粗抽出液を得る方法などが適宜用いられる。緩衝液の中に尿素や塩酸グアニジンなどのタンパク質変性剤や、トリトン X-100<sup>TM</sup>などの界面活性剤が含まれていてもよい。培養液中にレセプタータンパク質が分泌される場合には、培養終了後、公知の方法で菌体あるいは細胞と上清とを分離し、上清を集める。

このようにして得られた培養上清、あるいは抽出液中に含まれる融合タンパク質の精製は、公知の分離・精製法を適切に組み合わせて行なうことができる。これらの公知の分離、精製法としては、塩析や溶媒沈澱法などの溶解度を利用する方法、透析法、限外ろ過法、ゲルろ過法、および SDS-ポリアクリルアミドゲル電気泳動法などの主として分子量の差を利用する方法、イオン交換クロマトグラフィーなどの荷電の差を利用する方法、アフィニティークロマトグラフィーなどの特異的親和性を利用する方法、逆相高速液体クロマトグラフィーなどの疎水性の差を利用する方法、等電点電気泳動法などの等電点の差を利用する方法などが用いられる。

かくして得られる融合タンパク質が遊離体で得られた場合には、公知の方法あるいはそれに準じる方法によって塩に変換することができ、逆に塩で得られた場合には公知の方法あるいはそれに準じる方法により、遊離体または他の塩に変換することができる。

なお、組換え体が産生する融合タンパク質を、精製前または精製後に適当なタンパク質修飾酵素を作用させることにより、任意に修飾を加えたり、ポリペプチドを部分的に除去することもできる。タンパク質修飾酵素としては、例えば、トリプシン、キモトリプシン、アルギニルエンドペプチダーゼ、プロテインキナーゼ、グリコシダーゼなどが用いられる。

かくして生成する融合タンパク質またはその塩の活性または存在は、標識したリガンドとの結合実験および特異抗体を用いたエンザイムイムノアッセイなどにより測定することができる。

本発明のリガンドの決定方法に用いられる試験化合物としては、公知のリガンド（例えば、アンギオテンシン、ボンベシン、カナビノイド、コレシストキニン、グルタミン、セロトニン、メラトニン、ニューロペプチド Y、オピオイド、プ

リン、バソプレッシン、オキシトシン、PACAP（例、PACAP 27、PACAP 38）、セクレチン、グルカゴン、カルシトニン、アドレノメジュリン、ソマトスタチン、GHRH、CRF、ACTH、GRP、PTH、VIP（バソアクティブ・インテスティナル・アンド・リレイテッド・ポリペプチド）、ソマトスタチン、ドーパミン、モチリン、アミリン、ブラジキニン、CGRP（カルシトニンジーンリレーティッドペプチド）、ロイコトリエン、パンクレアスタチン、プロスタグランジン、トロンボキサン、アデノシン、アドレナリン、ケモカインスーパーファミリー（例、IL-8、GRO $\alpha$ 、GRO $\beta$ 、GRO $\gamma$ 、NAP-2、ENA-78、GCP-2、PF4、IP-10、Mig、PBSF/SDF-1などのCXCケモカインサブファミリー；MCAF/MCP-1、MCP-2、MCP-3、MCP-4、eotaxin、RANTES、MIP-1 $\alpha$ 、MIP-1 $\beta$ 、HCC-1、MIP-3 $\alpha$ /LARC、MIP-3 $\beta$ /ELC、I-309、TARC、MIPF-1、MIPF-2/eotaxin-2、MDC、DC-CK1/PARC、SLCなどのCCケモカインサブファミリー；lymphotactinなどのCケモカインサブファミリー；fractalkineなどのCX3Cケモカインサブファミリー等）、エンドセリン、エンテロガストリン、ヒスタミン、ニューロテンシン、TRH、パンクレアティックポリペプチド、ガラニン、リゾホスファチジン酸（LPA）、スフィンゴシン1-リン酸、リゾホスファチジルセリン、スフィンゴシルホスホリルコリン、リゾホスファチジルコリン、ステロイド類、胆汁酸類、イソプレノイド、アラキドン酸代謝物、アミン類、アミノ酸、ヌクレオチド、ヌクレオシド、飽和脂肪酸または不飽和脂肪酸など）の他に、例えば、ヒトまたは哺乳動物（例えば、マウス、ラット、ブタ、ウシ、ヒツジ、サルなど）の組織抽出物、細胞培養上清などが用いられる。例えば、該組織抽出物、細胞培養上清などを、オーファンレセプターとGFPとの融合タンパク質を発現させた細胞に添加し、その細胞刺激活性などを測定しながらスクリーニングを行い、最終的に単一のリガンドを決定することができる。

本発明のリガンド決定方法Aは、具体的には、該融合タンパク質の発現細胞を構築し、該発現細胞やその細胞膜画分を用いて細胞刺激活性アッセイやレセプタ

一結合アッセイを行うことによって、オーファンレセプターに結合して細胞刺激活性（例えば、アラキドン酸遊離、アセチルコリン遊離、細胞内 $Ca^{2+}$ 遊離、細胞内cAMP生成、細胞内cGMP生成、イノシトールリン酸産生、細胞膜電位変動、細胞内タンパク質のリン酸化、c-fos活性化、pHの低下などを促進する活性または抑制する活性）、MAPキナーゼの活性化、転写因子（例、CRE、AP1、NFkBなど）の活性化、ジアシルグリセロール産生、細胞膜上のイオンチャンネル（例、 $K^+$ 、 $Ca^{2+}$ 、 $Na^+$ 、 $Cl^-$ など）の開閉、アポトーシスの誘導、細胞の形態変化、レセプター（融合タンパク質）の細胞膜から細胞質への移行、低分子量Gタンパク質（例、Ras、Rap、Rho、Rabなど）の活性化、細胞分裂促進活性、DNA合成促進活性などを有する化合物、すなわちリガンド（例えば、ペプチド、タンパク質、非ペプチド性化合物、合成化合物、発酵生産物など）を決定する方法である。

本発明のリガンド決定方法は、融合タンパク質を発現している細胞またはその細胞膜画分と試験化合物とを接触させた場合の、例えば、該オーファンレセプターに対する試験化合物の結合量や細胞刺激活性などを測定することを特徴とする。

より具体的には、本発明は、次のようなりガンド決定方法を提供する。

（１）標識した試験化合物を、融合タンパク質を発現している細胞またはその細胞膜画分に接触させた場合における、標識した試験化合物の該細胞またはその細胞膜画分に対する結合量を測定することを特徴とするオーファンレセプターに対するリガンドの決定方法、

（２）標識した試験化合物を、融合タンパク質をコードするDNAを含有する形質転換体を培養することによって細胞膜上に発現した融合タンパク質に接触させた場合における、標識した試験化合物のオーファンレセプターに対する結合量を測定することを特徴とするオーファンレセプターに対するリガンドの決定方法

（３）試験化合物を、融合タンパク質を発現している細胞に接触させた場合における、オーファンレセプターを介した前記細胞刺激活性、MAPキナーゼの活性化、転写因子（例、CRE、AP1、NFkBなど）の活性化、ジアシルグリ

セロール産生、細胞膜上のイオンチャンネル（例、 $K^+$ 、 $Ca^{2+}$ 、 $Na^+$ 、 $Cl^-$ など）の開閉、アポトーシスの誘導、細胞の形態変化、レセプター（融合タンパク質）の細胞膜から細胞質への移行、低分子量Gタンパク質（例、Ras、Rap、Rho、Rabなど）の活性化、細胞分裂促進活性、DNA合成促進活性などを測定することを特徴とするオーファンレセプターに対するリガンドの決定方法、および

（４）試験化合物を、融合タンパク質をコードするDNAを含有する形質転換体を培養することによって細胞膜上に発現した融合タンパク質に接触させた場合における、オーファンレセプターを介する前記細胞刺激活性、MAPキナーゼの活性化、転写因子（例、CRE、AP1、NFkBなど）の活性化、ジアシルグリセロール産生、細胞膜上のイオンチャンネル（例、 $K^+$ 、 $Ca^{2+}$ 、 $Na^+$ 、 $Cl^-$ など）の開閉、アポトーシスの誘導、細胞の形態変化、レセプター（融合タンパク質）の細胞膜から細胞質への移行、低分子量Gタンパク質（例、Ras、Rap、Rho、Rabなど）の活性化、細胞分裂促進活性、DNA合成促進活性などを測定することを特徴とするオーファンレセプターに対するリガンドの決定方法を提供する。

特に、上記（１）～（２）の試験を行ない、試験化合物がオーファンレセプターに結合することを確認した後に、上記（３）～（４）の試験を行なうことが好ましい。

場合によっては、上記発現細胞から融合タンパク質を単離精製し、それを用いてレセプター結合アッセイ等を行うこともできる。リガンド決定方法に用いる融合タンパク質としては、前記細胞を用いて大量発現させた融合タンパク質が適している。

融合タンパク質を製造するには、上記の発現方法が用いられるが、該融合タンパク質をコードするDNAを哺乳動物細胞や昆虫細胞などで発現させることが好ましい。融合タンパク質をコードするDNA断片を宿主細胞に導入し、それらを効率よく発現させるためには、該DNA断片をバキュロウイルスに属する核多角体病ウイルス（nuclear polyhedrosis virus；NPV）のポリヘドリンプロモーター、SV40由来のプロモーター、レトロウイルスのプロモーター、メタロチ

オネインプロモーター、ヒトヒートショックプロモーター、サイトメガロウイルスプロモーター、SR $\alpha$ プロモーターなどの下流に組み込むのが好ましい。発現した融合タンパク質の量と質の検査は公知の方法で行うことができる。例えば、文献〔Nambi, P. ら、J. Biol. Chem., 267, 19555-19559 (1992)〕に記載の方法に従って行うことができる。

本発明のリガンド決定方法において、融合タンパク質を発現している細胞またはその細胞膜画分を用いるのが好ましい。

本発明のリガンド決定方法において、融合タンパク質を発現している細胞を用いる場合、該細胞をグルタルアルデヒド、ホルマリンなどで固定化してもよい。

10 固定化方法は公知の方法に従って行なうことができる。

融合タンパク質を発現している細胞とは、融合タンパク質を発現した宿主細胞をいうが、該宿主細胞としては、大腸菌、枯草菌、酵母、昆虫細胞、動物細胞などが用いられる。

細胞膜画分としては、細胞を破碎した後、公知の方法で得られる細胞膜が多く含まれる画分のことをいう。細胞の破碎方法としては、Potter-Elvehjem型ホモジナイザーで細胞を押し潰す方法、ワーリングブレンダーやポリトロン (Kinematica社製) による破碎、超音波による破碎、フレンチプレスなどで加圧しながら細胞を細いノズルから噴出させることによる破碎などが挙げられる。細胞膜の分画には、分画遠心分離法や密度勾配遠心分離法などの遠心力による分画法が主として用いられる。例えば、細胞破碎液を低速 (500rpm~3000rpm) で短時間 (通常、約1分~10分) 遠心し、上清をさらに高速 (15000rpm~30000rpm) で通常30分~2時間遠心し、得られる沈澱を膜画分とする。該膜画分中には、発現した融合タンパク質と細胞由来のリン脂質や膜タンパク質などの膜成分が多く含まれる。

25 該融合タンパク質を発現している細胞やその膜画分中の融合タンパク質の量は、1細胞当たり $10^3 \sim 10^8$ 分子であるのが好ましく、 $10^5 \sim 10^7$ 分子であるのが好適である。なお、発現量が多いほど膜画分当たりのリガンド結合活性 (比活性) が高くなり、高感度なスクリーニング系の構築が可能になるばかりでなく、同一ロットで大量の試料を測定できるようになる。この融合タンパク質の発

現量を、蛍光顕微鏡や蛍光光度計を用いて、細胞や細胞膜におけるGFP発光量から概算することができる。

5 オーフアンレセプターに対するリガンドを決定する上記の(1)～(2)の方法を実施するためには、融合タンパク質を含有する適当な細胞または細胞膜画分および標識した試験化合物が必要である。融合タンパク質画分としては、天然型のオーファンレセプターと同等の活性を有する組換え型融合レセプターを含有するものが望ましい。ここで、同等の活性とは、同等のリガンド結合活性、シグナル情報伝達作用などを示す。

10 標識した試験化合物として、 $[^3\text{H}]$ 、 $[^{125}\text{I}]$ 、 $[^{14}\text{C}]$ 、 $[^{35}\text{S}]$ などで標識した、前述のリガンド化合物群から選ばれる化合物が用いられる。

具体的には、本発明のリガンドの決定方法を行なうには、まず融合タンパク質を発現している細胞またはその細胞膜画分を、決定方法に適したバッファーに懸濁することにより融合タンパク質標品を調製する。バッファーには、pH4～10（望ましくはpH6～8）のリン酸バッファー、トリス-塩酸バッファーなどのリガンドとオーファンレセプターとの結合を阻害しないバッファーであればい  
15 ずれでもよい。また、非特異的結合を低減させる目的で、CHAPS、Tween-80<sup>TM</sup>（花王-アトラス社）、ジギトニン、デオキシコレートなどの界面活性剤やウシ血清アルブミンやゼラチンなどの各種タンパク質をバッファーに加えることもできる。さらに、プロテアーゼによるレセプターやリガンドの分解を抑える目的でPMSF、ロイペプチン、E-64（ペプチド研究所製）、ペプスタチンなどのプロテアーゼ阻害剤を添加することもできる。そして、例えば0.01ml～10mlの該レセプター標品に、一定量（5000cpm～500000cpm）の $[^3\text{H}]$ 、 $[^{125}\text{I}]$ 、 $[^{14}\text{C}]$ 、 $[^{35}\text{S}]$ などで標識した試験化合物を共存させる。非特異的結合量（NSB）を知るために大過剰の未標識の  
20 試験化合物を加えた反応チューブも用意する。反応は約0℃～50℃、望ましくは約4℃～37℃で、約20分～24時間、望ましくは約30分～3時間行なう。反応後、ガラス繊維濾紙等で濾過し、適量の同バッファーで洗浄した後、ガラス繊維濾紙に残存する放射活性を液体シンチレーションカウンターあるいはγ-カウンターで計測する。全結合量（B）から非特異的結合量（NSB）を引いた

カウント (B-N S B) が 0 c p m を越える試験化合物をオーファンレセプターに対するリガンド (アゴニストを含む) として選択することができる。

本発明のリガンドを決定する上記の (3) ~ (4) の方法を実施するためには、オーファンレセプターを介する前記細胞刺激活性、例えばMAPキナーゼの活性化、転写因子 (例、CRE、AP1、NF $\kappa$ Bなど) の活性化、ジアシルグリセロール産生、細胞膜上のイオンチャンネル (例、K<sup>+</sup>、Ca<sup>2+</sup>、Na<sup>+</sup>、Cl<sup>-</sup>など) の開閉、アポトーシスの誘導、細胞の形態変化、レセプター (融合タンパク質) の細胞膜から細胞質への移行、低分子量Gタンパク質 (例、Ras、Rap、Rho、Rabなど) の活性化、細胞分裂促進活性、DNA合成促進活性などを公知の方法または市販の測定用キットを用いて測定することができる。具体的には、まず、融合タンパク質を発現している細胞をマルチウェルプレート等に培養する。リガンド決定を行なうにあたっては前もって新鮮な培地あるいは細胞に毒性を示さない適当なバッファーに交換し、試験化合物などを添加して一定時間インキュベートした後、細胞を抽出あるいは上清液を回収して、生成した代謝産物をそれぞれの方法に従って定量する。細胞刺激活性の指標とする物質 (例えば、アラキドン酸など) の生成が、細胞が含有する分解酵素によって検定困難な場合は、該分解酵素に対する阻害剤を添加してアッセイを行なってもよい。また、cAMP産生抑制などの活性については、フォルスコリンなどで細胞の基礎的産生量を増大させておいた細胞に対する産生抑制作用として検出することができる。

上記細胞刺激活性のうち「レセプターの細胞質内への移行」の測定では、GFPなどの蛍光タンパク質の蛍光を測定することで、融合タンパク質の細胞膜から細胞質への移動を観察することができる。融合タンパク質の細胞膜から細胞質への移動の観察するためには、前記した融合タンパク質を安定的にまたは一過性に発現している動物細胞を用いるのが適している。適当な培養器に通常の培地を用いて培養した当該細胞に、適当な濃度に希釈した試験化合物を添加する。その際培地に直接希釈した試験化合物溶液を添加しても良いが、細胞をハンス平衡塩溶液 (HBSS、BSAを0から10%、好ましくは0.1から1%添加しても良い) で洗浄した後、試験化合物を含有する同液を添加しても良い。該細胞はリ

ガンド添加後、4℃から37℃、好ましくは20℃から37℃で1分から6時間、好ましくは10分から2時間放置後に、融合タンパク質の細胞膜から細胞質への移動を観察する。該細胞はそのままでも観察可能であるが、グルタルアルデヒドやホルマリンで固定してもよい。固定方法は公知の方法に従って行うことがで

5 きる。

観察は通常の蛍光顕微鏡や共焦点レーザー顕微鏡を用いればよいが、励起光を照射できる機能と蛍光像を取り込む機能を備えたプレートリーダーなども使用できる。その際、レセプターと、配列番号：3または配列番号：5で示した野生型GFPまたはGFPuvとの融合タンパク質を検出するためには紫外光、好ましくは395nmで励起し、フルオレセイン・イソシアネート（FITC）や一般  
10 に市販されるGFP検出用のフィルターを用いて観察できる。また、配列番号：1または配列番号：7で示したGFPとの融合タンパク質を検出するためには460～500nm、好ましくは488nmの励起光で励起し、FITCや一般に市販されるGFP検出用のフィルターを用いて観察すればよい。

15 レセプター（融合タンパク質）の細胞質内への移行の他に、レセプターの凝集、レセプターの局在化、あるいはレセプターの発現の低下または増加など、顕微鏡的に観察できるレセプターの形態学的な変化を観察することもできる。

本発明のリガンド決定法Bを実施する場合、融合タンパク質の発現ベクター以外に、特定のエンハンサー／プロモーターの下流にレポータータンパク質をコードするDNAを含有するプラスミドを、細胞、好ましくは真核生物由来の細胞に  
20 組み込むことが必要である。このプラスミドは、細胞、好ましくは真核生物由来の細胞内で該レポータータンパク質を発現させることのできるプロモーターを含有し、更に原核生物内で増殖させる場合の選択マーカーとして薬剤耐性遺伝子（例えば、アンピシリン耐性遺伝子）などを含有してもよい。

25 エンハンサー／プロモーターの下流にレポータータンパク質をコードするDNAを含有するプラスミドは、そのエンハンサーの制御下に細胞内でレポータータンパク質を発現することでき、かつ細胞内に導入できるプラスミドであれば、市販のプラスミドなどのいかなるプラスミドでもよい。

エンハンサーとしては、例えば、SV40、パピローマウイルス等のウイルス



由来のエンハンサー、レトロウイルスのLTR、cAMPレスポンスエレメント（cAMP応答配列）（CRE）、あるいはTPAレスポンスエレメント（TPA応答配列）（TRE）等が用いられ、好ましくはcAMPレスポンスエレメントである。該細胞が発現するオーファンレセプターによって仲介される上記細胞刺激活性によって活性化されるエンハンサーが適当である。

プロモーターとしては、例えば、SV40プロモーター、CMVプロモーター、HSVのチミジンキナーゼ遺伝子のTATA様プロモーター等が用いられ、好ましくはTATA様プロモーターである。

レポータータンパク質遺伝子としては、例えば、ルシフェラーゼ遺伝子、 $\beta$ -ガラクトシダーゼ遺伝子、GFP遺伝子、アルカリフォスファターゼ遺伝子等が用いられる。公知の方法にて酵素活性を検出できるような酵素遺伝子であれば、レポータータンパク質として用いる。

かかるプラスミドの具体例として、cAMPレスポンスエレメントの下流にTATA様プロモーターおよびレポータータンパク質（例、ルシフェラーゼ遺伝子）をコードする遺伝子を連結したプラスミド、例えばpCRE-Luc（Clontech社）などがある。

リガンド決定方法Bで用いられる細胞としては、前記した宿主細胞が用いられ、好ましくは真核生物由来の細胞、より好ましくは動物細胞（例、サル細胞COS-7、Vero、CHO細胞、CHO(dhfr<sup>-</sup>)細胞、マウスL細胞、マウスAtT-20、マウスミエローマ細胞、ラットGH3、ヒトFL細胞、ヒトHEK293細胞など）などが用いられる。

該細胞は、2種以上（好ましくは2～3種）の融合タンパク質を発現しているもよい。

2種類以上の融合タンパク質を発現させる場合は、類似の生物学的特徴を有する2種類以上のオーファンレセプターを用いるのが良い。

類似の特徴としては、例えば、使用する2種類以上のオーファンレセプターをそれぞれ単独で発現させた時のレポータータンパク質の発現量などが挙げられる。具体的には、2種類以上のオーファンレセプターをそれぞれ単独で発現させた場合における(1)レポータータンパク質の基礎発現量および/または(2)フォルス

コリン添加時のレポータータンパク質の発現量を指標として、各レセプタータンパク質の特徴を区別することができる。

従って、2種類以上のオーファンレセプターを発現させてリガンドを決定する場合、あらかじめレポータータンパク質の基礎発現量が低いもの、中程度のもの  
5、明らかに高いものなどに区分けをしたり、あるいはフォルスコリン添加によってレポータータンパク質の発現量が上昇しにくいレセプタータンパク質を明らかにしておくことが望ましい。なぜならば、例えばレポータータンパク質の基礎発現量が高いレセプタータンパク質とレポータータンパク質の基礎発現量が低いレセプターの2種類のレセプタータンパク質を発現させた場合、後者にリガンドが  
10結合した場合にレポータータンパク質発現量の上昇が検出しにくくなるからである。すなわち：

- (1) レポータータンパク質の基礎発現量が高いオーファンレセプターと低いレセプタータンパク質の混合は避けるのが好ましい、
- (2) フォルスコリン添加によるレポータータンパク質の発現量の上昇が顕著な  
15レセプタータンパク質とそうでないオーファンレセプターは混合しないほうが好ましい、
- (3) レポータータンパク質の基礎発現量が同程度であるオーファンレセプター同士を組み合わせ発現させるのが好ましい。

このように類似の特徴を有するオーファンレセプターの組合わせとしては、例  
20例えば、APJ（アペリンレセプター；Gene, 136, 355 (1993)）とTGR-1（特開2002-078492号）との組み合わせが挙げられる。

リガンドの決定方法Bの具体例を以下に記載する。

細胞を96ウェルプレートに播種し、例えば10%ウシ胎児血清を含むDMEMで一晩培養する。ここで、例えば市販のトランスフェクションキットを用いて  
25、融合タンパク質の発現プラスミドおよびレポータープラスミドを同時に細胞に導入し、細胞をさらに一晩培養することにより、細胞内でオーファンレセプターを一過性に発現させる。細胞を洗浄し、さらに培地を無血清化した後、試験化合物を添加する。エンハンサーがCREである場合、試験化合物と同時にフォルスコリンを添加してもよい。一定時間インキュベーションを行った後、細胞を溶解

し、レポータータンパク質の活性を測定する。

前記の決定方法において、レポータータンパク質活性のベースラインが高く、試験化合物による活性の変化の検出が困難な場合には、ベースラインを低下させる手段を講じるとよい。例えばオーファンレセプターがGタンパク質共役型レセ

- 5 プタータンパク質（GPCR）の場合、Gタンパク質の $\alpha$ サブユニットのうち、cAMP抑制効果を示すGiタンパク質を加えることにより、活性変化の検出が容易となる。Giタンパク質を発現させるために、Giタンパク質をコードするDNAを発現するプラスミドを、オーファンレセプタープラスミドおよびレポータープラスミドと共に細胞に導入することができる。この場合、3種のプラスミド（オーファンレセプタープラスミド：レポータープラスミド：Giプラスミド）の混合比は、好ましくは5～15：1：1～6程度、さらに好ましくは7：1：3程度である。

- 15 本発明のリガンド決定方法Bにおいて、試験化合物を添加した場合に、レポータータンパク質の活性が約20%以上、好ましくは約50%以上、上昇または減少した時、当該試験化合物をリガンドとして同定することができる。

本発明のリガンド決定方法Bにおいて用いられる試験化合物は、前述の試験化合物などから選択される化合物である。

更に、本発明のリガンド決定用キットは、本発明の融合タンパク質を発現し得る細胞またはその細胞膜画分などを含有するものである。

- 20 本発明のリガンド決定用キットの例としては、次のものが挙げられる。

1. リガンド決定用試薬

(1) 測定用緩衝液および洗浄用緩衝液

Hanks' Balanced Salt Solution（ギブコ社製）に、0.05%のウシ血清アルブミン（シグマ社製）を加えたもの。

- 25 孔径0.45  $\mu$ mのフィルターで濾過滅菌し、4℃で保存するか、あるいは用時調製しても良い。

(2) 融合タンパク質標品

融合タンパク質を発現しているCHO細胞を、12穴プレートに $5 \times 10^5$ 個/穴で継代し、37℃、5%CO<sub>2</sub>、95%airで2日間培養したもの。

## (3) 標識試験化合物

市販の [ $^3\text{H}$ ]、 [ $^{125}\text{I}$ ]、 [ $^{14}\text{C}$ ]、 [ $^{35}\text{S}$ ] などで標識した化合物、または適当な方法で標識化したもの。

- 5 水溶液の状態のものを  $4^\circ\text{C}$  あるいは  $-20^\circ\text{C}$  にて保存し、用時に測定用緩衝液にて  $1\ \mu\text{M}$  に希釈する。水に難溶性を示す試験化合物については、ジメチルホルムアミド、DMSO、メタノール等に溶解する。

## (4) 非標識試験化合物

標識化合物と同じものを  $100\sim 1000$  倍濃い濃度に調製する。

## 2. 測定法

- 10 (1)  $12$  穴組織培養用プレートにて培養した本発明のレセプタータンパク質発現CHO細胞を、測定用緩衝液  $1\text{ ml}$  で2回洗浄した後、 $490\ \mu\text{l}$  の測定用緩衝液を各穴に加える。

(2) 標識試験化合物を  $5\ \mu\text{l}$  加え、室温にて1時間反応させる。非特異的結合量を知るためには非標識試験化合物を  $5\ \mu\text{l}$  加えておく。

- 15 (3) 反応液を除去し、 $1\text{ ml}$  の洗浄用緩衝液で3回洗浄する。細胞に結合した標識試験化合物を  $0.2\text{ N NaOH}-1\% \text{ SDS}$  で溶解し、 $4\text{ ml}$  の液体シンチレーターA（和光純薬製）と混合する。

(4) 液体シンチレーションカウンター（ベックマン社製）を用いて放射活性を測定する。

- 20 この様に、本発明のリガンド決定方法（A及びB）によれば、GFPなどの蛍光タンパク質の蛍光またはGFP抗体などの蛍光タンパク質抗体を利用した免疫染色法やウエスタンブロット法など用いて、

(1) タンパク質レベルでレセプタータンパク質が発現していることを確認でき

- 25 (2) 細胞膜にレセプタータンパク質が発現していることを確認でき、

(3) レセプタータンパク質の発現量を見積もることができ、

(4) レセプタータンパク質の高発現細胞を選択でき、そして

(5) リガンドによるレセプターの特異的反応を、レセプターと蛍光タンパク質との融合タンパク質の細胞内へのインターナリゼーションとして検出できる。こ

れらの特徴を利用することにより、リガンドが決定されていないレセプタータンパク質（オーファンレセプター）のリガンドを効率よく決定できる。

- このようにして決定されたリガンドは、そのレセプタータンパク質に結合して、その生理的機能を調節するので、そのレセプタータンパク質の機能に関連する疾患の予防及び／又は治療剤として用いることができる。さらには、リガンドとそのレセプタータンパク質を用いて、該レセプターのアゴニスト／アンタゴニストのスクリーニングを行うことができる。

- 本明細書および図面において、塩基やアミノ酸などを略号で表示する場合、IUPAC-IUB Commission on Biochemical Nomenclature による略号あるいは当該分野における慣用略号に基づく。またアミノ酸に関し光学異性体があり得る場合は、特に明示しなければL体を示すものとする。

本明細書の配列表の配列番号は、以下の配列を示す。

配列番号：1

- 15 実施例1で使用したGFP（以下、GFP-1と略記する）のアミノ酸配列を示す。

配列番号：2

実施例1で使用したGFPをコードするDNAの塩基配列を示す。

配列番号：3

- 20 野生型GFPのアミノ酸配列を示す。

配列番号：4

野生型GFPをコードするDNAの塩基配列を示す。

配列番号：5

GFPuvのアミノ酸配列を示す。

- 25 配列番号：6

GFPuvをコードするDNAの塩基配列を示す。

配列番号：7

EGFPのアミノ酸配列を示す。

配列番号：8

E G F Pをコードするc D N Aの塩基配列を示す。

配列番号：9

実施例1で用いるヒト由来Gタンパク質共役型レセプタータンパク質T G R 5  
のアミノ酸配列を示す。

5 配列番号：10

実施例1で用いるヒト由来Gタンパク質共役型レセプタータンパク質T G R 5  
をコードするc D N Aの塩基配列を示す。

配列番号：11

参考例1におけるP C R反応で使用したプライマー1の塩基配列を示す。

10 配列番号：12

参考例1におけるP C R反応で使用したプライマー2の塩基配列を示す。

配列番号：13

ヒト由来副甲状腺ホルモン受容体（P T H-R）のアミノ酸配列を示す。

配列番号：14

15 ヒト由来副甲状腺ホルモン受容体（P T H-R）をコードするc D N Aの塩基  
配列を示す。

配列番号：15

ヒト由来G P R 40のアミノ酸配列を示す。

配列番号：16

20 ヒト由来G P R 40をコードするc D N Aの塩基配列を示す。

配列番号：17

H i s - T a gのアミノ酸配列を示す。

配列番号：18

V 5 - t a gのアミノ酸配列を示す。

25 配列番号：19

m y c - t a gのアミノ酸配列を示す。

配列番号：20

X p r e s s - t a gのアミノ酸配列を示す。

配列番号：21

HA-t a gのアミノ酸配列を示す。

配列番号：22

ECFPのアミノ酸配列を示す。

配列番号：23

- 5 ECFPをコードするcDNAの塩基配列を示す。

配列番号：24

EYFPのアミノ酸配列を示す。

配列番号：25

EYFPをコードするcDNAの塩基配列を示す。

- 10 配列番号：26

DsREDのアミノ酸配列を示す。

配列番号：27

DsREDをコードするcDNAの塩基配列を示す。

配列番号：28

- 15 EBFPAのアミノ酸配列を示す。

配列番号：29

EBFPAをコードするcDNAの塩基配列を示す。

配列番号：30

- 20 オーフアンレセプターhBL5とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：31

オーファンレセプターh7TBA62とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：32

- 25 オーフアンレセプター14273とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：33

オーファンレセプターEMR3とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：34

オーファンレセプターGPR15とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：35

- 5 オーファンレセプターGPR31とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：36

オーファンレセプターGPCR5BとGFP-1との融合タンパク質のアミノ酸配列を示す。

- 10 配列番号：37

オーファンレセプターPSEC0142とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：38

- 15 オーファンレセプターHE6とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：39

オーファンレセプターGPR61とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：40

- 20 オーファンレセプターTGR9とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：41

オーファンレセプターTGR24とGFP-1との融合タンパク質のアミノ酸配列を示す。

- 25 配列番号：42

オーファンレセプターZGPR1とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：43

オーファンレセプターEMR1とGFP-1との融合タンパク質のアミノ酸配



列を示す。

配列番号：44

オーファンレセプターGPR25とGFP-1との融合タンパク質のアミノ酸配列を示す。

5 配列番号：45

オーファンレセプターGPR55とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：46

10 オーファンレセプターAXOR14とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：47

オーファンレセプターTM7SF1とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：48

15 オーファンレセプターPSP24BとGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：49

オーファンレセプターSREB3とGFP-1との融合タンパク質のアミノ酸配列を示す。

20 配列番号：50

オーファンレセプターTGR37とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：51

25 オーファンレセプターH963とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：52

オーファンレセプターGPR87とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：53

オーファンレセプターGPR91とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：54

5 オーファンレセプターPNRとGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：55

オーファンレセプターTGR29とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：56

10 オーファンレセプターTGR36とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：57

オーファンレセプターH9とGFP-1との融合タンパク質のアミノ酸配列を示す。

15 配列番号：58

オーファンレセプターTGR18とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：59

20 オーファンレセプターTGR19とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：60

オーファンレセプターAM-RとGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：61

25 オーファンレセプターGPR19とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：62

オーファンレセプターGPR45とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：63

オーファンレセプターGPRC5DとGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：64

- 5 オーファンレセプターLGR6とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：65

オーファンレセプターRUP3とGFP-1との融合タンパク質のアミノ酸配列を示す。

- 10 配列番号：66

オーファンレセプターTGR14とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：67

- 15 オーファンレセプターTPRA40とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：68

オーファンレセプターGPR22とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：69

- 20 オーファンレセプターGPR52とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：70

オーファンレセプターFLH2882とGFP-1との融合タンパク質のアミノ酸配列を示す。

- 25 配列番号：71

オーファンレセプターSNORF36とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：72

オーファンレセプターMRGとGFP-1との融合タンパク質のアミノ酸配列

を示す。

配列番号：73

オーファンレセプターSREB2とGFP-1との融合タンパク質のアミノ酸配列を示す。

5 配列番号：74

オーファンレセプターGPR12とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：75

10 配列番号：76  
オーファンレセプターGPR30とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：77

15 配列番号：78  
オーファンレセプターGPR82とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：79

20 配列番号：80  
オーファンレセプターRECAPとGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：81

25 配列番号：82  
オーファンレセプターHB954とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：83

30 配列番号：84  
オーファンレセプターRDC1とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：85

35 配列番号：86  
オーファンレセプターTGR6とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：87

40 配列番号：88  
オーファンレセプターA-2とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：89

オーファンレセプターJEG18とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：83

- 5 オーファンレセプターGPR17とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：84

オーファンレセプターGPR35とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：85

- 10 オーファンレセプターGPCR5CとGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：86

オーファンレセプターHM74とGFP-1との融合タンパク質のアミノ酸配列を示す。

- 15 配列番号：87

オーファンレセプターRPEとGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：88

- 20 オーファンレセプターTGR13とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：89

オーファンレセプターTGR27とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：90

- 25 オーファンレセプターDEZとGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：91

オーファンレセプターratGPR1とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号： 9 2

オーファンレセプターGPR3とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号： 9 3

- 5     オーファンレセプターGPR6とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号： 9 4

オーファンレセプターRAIG1とGFP-1との融合タンパク質のアミノ酸配列を示す。

- 10    配列番号： 9 5

オーファンレセプターTGR2-1とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号： 9 6

- 15    オーファンレセプターTGR2-2とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号： 9 7

オーファンレセプターTGR21とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号： 9 8

- 20    オーファンレセプターGPR56とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号： 9 9

オーファンレセプターKIAA0758とGFP-1との融合タンパク質のアミノ酸配列を示す。

- 25    配列番号： 1 0 0

オーファンレセプターRE2とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号： 1 0 1

オーファンレセプターP40とGFP-1との融合タンパク質のアミノ酸配列

を示す。

配列番号：102

オーファンレセプターGPR27とGFP-1との融合タンパク質のアミノ酸配列を示す。

5 配列番号：103

オーファンレセプターHG38とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：104

10 オーファンレセプターDRR1とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：105

オーファンレセプターTGR12とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：106

15 オーファンレセプターTGR11とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：107

オーファンレセプターTGR15とGFP-1との融合タンパク質のアミノ酸配列を示す。

20 配列番号：108

オーファンレセプターTGR8とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：109

25 オーファンレセプターGPR20とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：110

オーファンレセプターTGR10とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：111

オーファンレセプターTGR30とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：112

- 5 オーファンレセプターGPR18とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：113

オーファンレセプターTGR25とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：114

- 10 オーファンレセプターGPR23とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：115

オーファンレセプターP2Y10とGFP-1との融合タンパク質のアミノ酸配列を示す。

- 15 配列番号：116

オーファンレセプターGPR37とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：117

- 20 オーファンレセプターET(B)R-LP-2とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：118

オーファンレセプターFPRL2とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：119

- 25 オーファンレセプターGPR32とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：120

オーファンレセプターdj287G14.2とGFP-1との融合タンパク質のアミノ酸配列を示す。



配列番号：1 2 1

オーファンレセプターBRS-3とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：1 2 2

- 5     オーファンレセプターGPR39とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：1 2 3

オーファンレセプター63A2とGFP-1との融合タンパク質のアミノ酸配列を示す。

- 10    配列番号：1 2 4

オーファンレセプターGPR84とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：1 2 5

- 15    オーファンレセプターGPR21とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：1 2 6

オーファンレセプターGPR48とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：1 2 7

- 20    オーファンレセプターSNORF1とGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：1 2 8

オーファンレセプターBA12とGFP-1との融合タンパク質のアミノ酸配列を示す。

- 25    配列番号：1 2 9

オーファンレセプターMASとGFP-1との融合タンパク質のアミノ酸配列を示す。

配列番号：1 3 0

オーファンレセプターOT7T009とGFP-1との融合タンパク質のアミ

ノ酸配列を示す。

配列番号：131

オーファンレセプターTGR34とGFP-1との融合タンパク質のアミノ酸配列を示す。

5 配列番号：132

オーファンレセプターhBL5とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：133

10 オーファンレセプターh7TBA62とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：134

オーファンレセプター14273とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：135

15 オーファンレセプターEMR3とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：136

オーファンレセプターGPR15とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

20 配列番号：137

オーファンレセプターGPR31とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：138

25 オーファンレセプターGPRC5BとGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：139

オーファンレセプターPSEC0142とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：140

オーファンレセプターHE 6 とGFP-1 との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：141

- 5      オーファンレセプターGPR 61 とGFP-1 との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：142

オーファンレセプターTGR 9 とGFP-1 との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：143

- 10      オーファンレセプターTGR 24 とGFP-1 との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：144

オーファンレセプターZGPR 1 とGFP-1 との融合タンパク質をコードするDNAの塩基配列を示す。

- 15      配列番号：145

オーファンレセプターEMR 1 とGFP-1 との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：146

- 20      オーファンレセプターGPR 25 とGFP-1 との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：147

オーファンレセプターGPR 55 とGFP-1 との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：148

- 25      オーファンレセプターAXOR 14 とGFP-1 との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：149

オーファンレセプターTM7SF 1 とGFP-1 との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：150

オーファンレセプターPSP24BとGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：151

- 5 オーファンレセプターSREB3とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：152

オーファンレセプターTGR37とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

- 10 配列番号：153

オーファンレセプターH963とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：154

- 15 オーファンレセプターGPR87とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：155

オーファンレセプターGPR91とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：156

- 20 オーファンレセプターPNRとGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：157

オーファンレセプターTGR29とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

- 25 配列番号：158

オーファンレセプターTGR36とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：159

オーファンレセプターH9とGFP-1との融合タンパク質をコードするDN

Aの塩基配列を示す。

配列番号：160

オーファンレセプターTGR18とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

5 配列番号：161

オーファンレセプターTGR19とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：162

10 オーファンレセプターAM-RとGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：163

オーファンレセプターGPR19とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：164

15 オーファンレセプターGPR45とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：165

オーファンレセプターGPRC5DとGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

20 配列番号：166

オーファンレセプターLGR6とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：167

25 オーファンレセプターRUP3とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：168

オーファンレセプターTGR14とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：169

オーファンレセプターTPRA40とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：170

- 5      オーファンレセプターGPR22とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：171

オーファンレセプターGPR52とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：172

- 10     オーファンレセプターFLH2882とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：173

オーファンレセプターSNORF36とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

- 15     配列番号：174

オーファンレセプターMRGとGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：175

- 20     オーファンレセプターSREB2とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：176

オーファンレセプターGPR12とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：177

- 25     オーファンレセプターGPR30とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：178

オーファンレセプターGPR82とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：179

オーファンレセプターRECAPとGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：180

- 5 オーファンレセプターHB954とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：181

オーファンレセプターRDC1とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

- 10 配列番号：182

オーファンレセプターTGR6とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：183

- 15 オーファンレセプターA-2とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：184

オーファンレセプターJEG18とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：185

- 20 オーファンレセプターGPR17とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：186

オーファンレセプターGPR35とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

- 25 配列番号：187

オーファンレセプターGPRC5CとGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：188

オーファンレセプターHM74とGFP-1との融合タンパク質をコードする

DNAの塩基配列を示す。

配列番号：189

オーファンレセプターRPEとGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

5 配列番号：190

オーファンレセプターTGR13とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：191

10 オーファンレセプターTGR27とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：192

オーファンレセプターDEZとGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：193

15 オーファンレセプターratGPR1とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：194

オーファンレセプターGPR3とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

20 配列番号：195

オーファンレセプターGPR6とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：196

25 オーファンレセプターRAIG1とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：197

オーファンレセプターTGR2-1とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：198



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オーファンレセプターTGR 2-2とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：199

- 5    オーファンレセプターTGR 21とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：200

オーファンレセプターGPR 56とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：201

- 10    オーファンレセプターKIAA 0758とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：202

オーファンレセプターRE 2とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

- 15    配列番号：203

オーファンレセプターP 40とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：204

- 20    オーファンレセプターGPR 27とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：205

オーファンレセプターHG 38とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：206

- 25    オーファンレセプターDRR 1とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：207

オーファンレセプターTGR 12とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：208

オーファンレセプターTGR11とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：209

- 5 オーファンレセプターTGR15とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：210

オーファンレセプターTGR8とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

- 10 配列番号：211

オーファンレセプターGPR20とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：212

- 15 オーファンレセプターTGR10とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：213

オーファンレセプターTGR30とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：214

- 20 オーファンレセプターGPR18とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：215

オーファンレセプターTGR25とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

- 25 配列番号：216

オーファンレセプターGPR23とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：217

オーファンレセプターP2Y10とGFP-1との融合タンパク質をコードす

るDNAの塩基配列を示す。

配列番号：218

オーファンレセプターGPR37とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

5 配列番号：219

オーファンレセプターET(B)R-LP-2とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：220

10 オーファンレセプターFPRL2とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：221

オーファンレセプターGPR32とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：222

15 オーファンレセプターdj287G14.2とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：223

オーファンレセプターBRS-3とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

20 配列番号：224

オーファンレセプターGPR39とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：225

25 オーファンレセプター63A2とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：226

オーファンレセプターGPR84とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：227

オーファンレセプターGPR21とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：228

- 5 オーファンレセプターGPR48とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：229

オーファンレセプターSNORF1とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：230

- 10 オーファンレセプターBA12とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：231

オーファンレセプターMASとGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

- 15 配列番号：232

オーファンレセプターOT7T009とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

配列番号：233

- 20 オーファンレセプターTGR34とGFP-1との融合タンパク質をコードするDNAの塩基配列を示す。

- 25 参考例1で得られた形質転換体エシェリヒア・コリ (*Escherichia coli*) JM109/pCR4-hTGR5は、平成12(2000)年4月3日から茨城県つくば市東1丁目1番地1 中央第6(郵便番号305-8566)の独立行政法人産業技術総合研究所 特許生物寄託センター(旧 通商産業省工業技術院生命工学工業技術研究所(NIBH))に寄託番号FERM BP-7114として、また平成12(2000)年3月23日から大阪府大阪市淀川区十三本町2丁目17番85号(郵便番号532-8686)の財団法人・発酵研究所(IFO)に寄託番号IFO 16410として寄託されている。

### 実施例

以下に参考例および実施例を示して、本発明をより詳細に説明するが、これらは本発明の範囲を限定するものではない。なお、大腸菌を用いての遺伝子操作は、モレキュラー・クローニング (Molecular cloning) に記載されている方法に従った。

#### 参考例 1 ヒト脾臓の G タンパク質共役型レセプタータンパク質をコードする cDNA のクローニングと塩基配列の決定

- 10 ヒト脾臓 cDNA (Clontech) を鋳型とし、2 個のプライマー、プライマー 1 (配列番号: 11) およびプライマー 2 (配列番号: 12) を用いて PCR 反応を行った。該反応における反応液の組成は、上記鋳型 cDNA 1/10 量、Advantage-GC2 Polymerase Mix (Clontech) 1/50 量、プライマー 1 (配列番号: 11) およびプライマー 2 (配列番号: 12) 各 0.5  $\mu$ M、dNTPs 200  $\mu$ M、および該酵素製品に添付のバッファー 1/5 量、GC Melt 1/5 量からなり、最終量を 20  $\mu$ l とした。PCR 反応では、94℃・5 分の後、94℃・30 秒、60℃・30 秒、68℃・2 分のサイクルを 30 回繰り返し、最後に 68℃・5 分の伸長反応を行った。該 PCR 反応産物を TA クローニングキット (Invitrogen) の処方に従いプラスミドベクター
- 20 pCR4 (Invitrogen) へサブクローニングした。これを大腸菌 JM109 に導入し、該 PCR 産物の cDNA を持つクローンをアンピシリンを含む LB 寒天培地中で選択した。個々のクローンの配列を解析した結果、新規 G タンパク質共役型レセプタータンパク質をコードする cDNA 配列 (配列番号: 10) を得た。この cDNA 配列から推定されるアミノ酸配列 (配列番号: 9) を有する新規 G タンパク質共役型レセプタータンパク質を TGR5 と命名した。また配列番号: 10 で表わされる DNA を含有する形質転換体が大腸菌 (*Escherichia coli*) JM109/pCR4-hTGR5 と命名した。
- 25

#### 参考例 2 TGR5 を一過性に発現させたヒト HEK293 細胞における、コレ

ステロール代謝関連物質によるレポーター活性化の検出

コレステロール代謝関連物質によるTGR 5特異的な刺激活性の検出は、CREプロモーターの発現誘導によって産生されるレポーター遺伝子産物（ルシフェラーゼ）の発現量を指標に行った。

- 5 ヒト由来のHEK 293細胞を増殖培地（DMEM（Dulbecco's Modified Eagle Medium）（GibcoBRL）に10%ウシ胎児血清（GibcoBRL）を添加したもの）に懸濁し、 $1 \times 10^5$  cells/wellの濃度にてコラーゲンでコートされたBlack well 96ウェルプレート（ベクトンディッキンソン社）にまいた。37℃、5%CO<sub>2</sub>条件下で一晩培養した後、レポーター遺伝子を含む
- 10 るプラスミドpCRE-Luc（Clontech）と共に、公知の方法により動物細胞用発現ベクターpAKKO-111H（Biochem. Biophys. Acta, Hinuma, S. et al., 1219, 251-259, 1994記載のpAKKO-1. 111Hと同一のプラスミドベクター）にTGR 5遺伝子を挿入して作製したTGR 5発現ベクタープラスミド、または、TGR 5遺伝子を含まない元のpAKKO-111Hを該細胞に
- 15 以下の通りにトランスフェクションした。

- OPTI-MEM-I（GibcoBRL）とLipofectamine™ 2000 試薬（GibcoBRL）を24:1にて混合することにより、リポフェクトアミン希釈液を調製した。また、OPTI-MEM-I、TGR 5発現ベクタープラスミドまたは元のベクタープラスミド（240 ng/μl）およびpCRE-Luc
- 20 c（240 ng/μl）を24:0.9:0.1にて混合することによりDNA希釈液を調製した。リポフェクトアミン希釈液とDNA希釈液を等量混合し、20分間室温で静置することによりDNAとリポフェクトアミンの複合体を形成させた後、その溶液25 μlを上記のHEK 293細胞を培養したプレートに添加し、さらに37℃、5%CO<sub>2</sub>条件下で一晩培養した。

- 25 トランスフェクトしたHEK 293細胞をアッセイ用培地（DMEMに0.1%ウシ血清アルブミンを添加したもの）にて洗浄した後、アッセイ用培地にて希釈したリトコール酸（和光純薬）およびプロゲステロン（和光純薬）を $2 \times 10^{-5}$  Mとなるようプレートに添加し、37℃、5%CO<sub>2</sub>条件下で4時間培養した。培養上清を捨てて、ルシフェラーゼ活性測定用の基質であるピッカジーンLT

2. 0 (東洋インキ製造株式会社) を  $50 \mu\text{l}$  添加し、プレートリーダー (ARVO s x マルチラベルカウンター、Wallac 社) を用いてルシフェラーゼの発光量を測定した。

5 その結果、配列番号: 10 で表される塩基配列を有する TGR5 遺伝子を導入した HEK293 細胞特異的に、リトコール酸およびプロゲステロンによるルシフェラーゼ活性の上昇が認められた (図 1)。

参考例 3 Gタンパク質共役型レセプタータンパク質発現プラスミドおよびレポータープラスミドの宿主細胞への導入

10 公知の方法によって作製した各種 Gタンパク質共役型レセプタータンパク質 cDNA、すなわち甲状腺ホルモン刺激因子レセプター (TRHR)、ニューロメジン Uレセプター (FM-3 および TGR-1)、プロラクチン放出因子レセプター (hGR3)、アペリンレセプター (APJ) などを挿入した動物細胞用発現プラスミドを用いて、大腸菌 JM109 を形質転換し、得られたコロニーを単  
15 離・培養後、QIAGEN Plasmid Maxi Kit (キアゲン) を用いてプラスミドの調製を行なった。また、cAMP レスポンスエレメント (CRE) の下流にレポーターとしてルシフェラーゼ遺伝子が連結された pCRE-Luc (Clontech) のレポータープラスミドを同様にして調製した。

Gタンパク質共役型レセプタータンパク質発現プラスミドおよびレポータープ  
20 ラスミドを導入する宿主細胞として、ヒト HEK293 細胞を I 型コラーゲンでコートした 96 ウェル黒色プレート (ベクトンディッキンソン社) に 100,000 cells/well、培養液量  $100 \mu\text{l}$  で播種し、一晚培養した。同じく CHO (dhfr<sup>-</sup>) 細胞を pAKK0-111H で形質転換した CHO-mock 細胞をコスター社の 96 ウェル黒色プレートに 40,000 cells/well、培養液量  $100 \mu\text{l}$  で播種し、  
25 一晚培養した。いずれの細胞についても、プレート培養するための培地として DMEM (GibcoBRL 社) に 10% のウシ胎児血清のみを添加したものを用了。

上記各プラスミドを  $240 \text{ ng}/\mu\text{l}$  の濃度に希釈し、Gタンパク質共役型レセプタータンパク質の発現プラスミド  $9 \mu\text{l}$  とレポータープラスミド  $1 \mu\text{l}$  の割合で  $240 \mu\text{l}$  の Opti-MEM-I (GibcoBRL 社) に添加した。これを、同じく  $240$

$\mu$ lのOpti-MEM-Iに10 $\mu$ lのリポフェクトアミン2000 (GibcoBRL社) を添加したものと等量混合して、リポフェクトアミン2000に添付の説明書の方法に従ってリポソームとプラスミドとの複合体を形成させた。また、効率的なスクリーニングの実施のためには、240 ng/ $\mu$ lの濃度で3種類のレセプター発現プラスミドを5 $\mu$ lずつ添加し、他の試薬の比率は前出と同じものを調製した。これらを25 $\mu$ l/wellずつHEK293あるいはCHO-mock細胞の培養液に添加し、37℃で一晩培養してプラスミドの導入を行った。CHO-mock細胞については、プラスミド添加後4時間以降に培養液をアッセイバッファー(0.1%のウシ血清アルブミンを添加したDMEM)に交換し、無血清化をおこなった。

#### 参考例4 レポーターアッセイによるリガンド活性の検出

HEK293細胞についてはアッセイの1時間前に培養液を、参考例3に記載のアッセイバッファーに交換し、プレインキュベーションを行なった。アッセイバッファーにリガンドあるいはリガンド候補化合物を溶解したものを用意し、参考例3で準備したHEK293細胞またはCHO-mock細胞に添加した。また、アッセイバッファーに終濃度2 $\mu$ Mのフォルスコリンを添加した条件でのアッセイも同様にして実施した。リガンドまたは試験化合物の添加後4時間のインキュベーションを行ない、レセプターを介したリガンドのアゴニスト活性によって惹起される細胞内シグナル伝達に由来するレポーター遺伝子の転写・翻訳の促進あるいは抑制を誘導した。インキュベーション終了後に各ウェルのアッセイバッファーを除去し、ピッカジーンLT2.0 (東洋インキ社) 発光基質を50 $\mu$ lずつ加えた。細胞が溶解し、基質と十分に混合した後、各ウェルのレポーター遺伝子の発現誘導量に相当する発光量を参考例2記載のプレートリーダーにて測定した。

参考例3および4に記載の方法に従って各種のGタンパク質共役型レセプタータンパク質cDNAを挿入した発現プラスミドを用い、HEK293細胞においてリガンド刺激によるレポーター遺伝子の発現誘導を測定した。細胞内へシグナルを伝達するGタンパク質の $\alpha$ サブユニットとしてGsに共役するCRFRにつ



いては、フォルスコリン非添加、添加のいずれの条件においてもリガンド添加によるレポーター遺伝子の活性化が検出された。また、抑制性であるG iに共役するAP Jについては、フォルスコリン添加条件において、リガンド添加によるレポーター遺伝子発現の抑制が検出された。また、G qに共役するレセプターTR HR、FM-3、TGR-1については、フォルスコリン添加条件においてレポーター遺伝子の発現の促進が検出された。G qおよびG iの両方に共役するレセプターhGR3についても、同様にフォルスコリン添加条件においてレポーター遺伝子の発現の促進が検出された（図2）。

10 参考例5 抑制性Gタンパク質 $\alpha$ サブユニットG i発現プラスミドを用いたレポーターアッセイ

参考例3に示したGタンパク質レセプター発現プラスミドと同様の方法によって、抑制性Gタンパク質 $\alpha$ サブユニット(G i)の発現プラスミドを調製した（ここで、G iについては、動物種を問わない）。これを3  $\mu$  l、レセプター発現プラスミドを7  $\mu$  l、レポータープラスミドを1  $\mu$  lの割合で240  $\mu$  lのOpti-ME M-Iに添加し、その他の条件は実施例2と同様の方法でHEK293あるいはCHO-mock細胞にDNAを導入した。これら3種のプラスミドの混合比は全体の量を11  $\mu$  lとした場合、G iが1から6  $\mu$  l、好ましくは1から3  $\mu$  lが適当である。これらを実施例3の方法に従ってアッセイを行いリガンド活性を検出した。

すなわち、G i共存下でのTGR5のリトコール酸に対する反応を検出した結果、CHO-mock細胞を用いたGタンパク質レセプターTGR5のアッセイにおいて、G iをTGR5と同時に発現させることにより、リガンド非添加時（リガンド（-））のルシフェラーゼ活性を大幅に低下させることができ、その結果リガンド（リトコール酸、 $2 \times 10^{-5}$ M、リガンド（+））による活性の上昇を検出することが可能となった（図3）。

実施例1 CHO細胞に発現させたTGR5-GFP融合タンパク質のタウロリトコール酸添加による細胞内移行

TGR5のC末端にオワンクラゲより単離されたGreen Fluorescent Protein (GFP)をつないだ融合タンパク質を発現させるための発現プラスミドを構築した。その際GFPのcDNA (配列番号: 2) としてGFPの発現ベクターpQBI25 (宝酒造) から切り出した断片を用いた。TGR5のcDNAはPCR法によりその終止コドン制限酵素Nhe Iの認識配列に修正し、ここにGFPのcDNA断片を連結して、実施例1に記載の発現ベクターpAKKO-111Hに挿入した。このようにして得たTGR5とGFPとの融合タンパク質 (以下、TGR5-GFP) の発現ベクタープラスミドを以下の方法でCHO-mock細胞にトランスフェクションした。CHO-mock細胞は増殖培地 [DMEM (Dulbecco's Modified Eagle Medium) (GIBCO BRL社) に10%ウシ胎児血清 (GIBCO BRL社) を添加したもの] に懸濁し、 $0.6 \times 10^5$  cells/チャンバーの濃度にてチャンバー数4つのLab-Tek IIカバーガラスチャンバー (Nalgen Nunc社) にまき、37℃、5%CO<sub>2</sub>条件下で一晩培養した後にトランスフェクションした。トランスフェクションにはLipofectamine™ 2000試薬 (GIBCO BRL社) を用いた。まず、Lipofectamine™ 2000 試薬 2μlとOPTI-MEM-I (GIBCO BRL社) 50μlを混合し、5分間放置後、これを0.48μgのDNAとOPTI-MEM-I 50μlの混合液と混ぜ合わせ、20分間室温で静置することによりDNAとリポフェクトアミンの複合体を形成させた。この混合液を上記のCHO細胞を培養したチャンバーに100μl添加し、さらに37℃、5%CO<sub>2</sub>条件下で一晩培養した。培地を共焦点顕微鏡観察用培地 [Hanks' Balanced Salt Solution (GIBCO BRL社) に0.1%ウシアルブミン (Essentially Fatty Acid Free (GIBCO BRL社)) を懸濁したもの] に置き換え、共焦点顕微鏡 (ライカ社) でGFPの蛍光像を観察した。その際、GFPの励起は488nmで行った。

その結果TGR5-GFP融合タンパク質は細胞膜に観察された (図4)。この細胞にタウロリトコール酸を $10^{-5}$ Mとなるように培地に添加した30分後には、GFPの蛍光が細胞膜ではなく、細胞質に移動していることが見出された

(図5)。このことはTGR5が細胞膜に発現するGタンパク質共役型のレセプターであるとともに、TGR5がタウロリトコール酸に反応して細胞質へ移行、すなわちインタナリゼーションしたことを示す。

5 実施例2 膵臓β細胞株RINm5Fに一過性発現による副甲状腺ホルモン受容体(PTH-R)とGFP融合タンパク質の発現

実施例1と同様の方法でヒトPTH-R(配列番号:13)のC末端にGFPをつないだ融合タンパク質を発現させるための発現プラスミドを参考例2に記載の発現ベクターpAKKO-111Hに挿入した発現ベクターを作製した。この  
10 ようにして得たPTH-RとGFPとの融合タンパク質(以下、PTH-GFP)の発現ベクタープラスミドを以下の方法でRINm5F細胞にトランスフェクションした。RINm5F細胞は増殖培地[RPMI1640(GIBCO BRL社)にCharcoal/Dextran処理済のウシ胎児血清(Hyclone社)を10%添加したもの]に懸濁し、 $0.3 \times 10^5$  cells/チェン  
15 ンバーの濃度にてチェンバー数8つのLab-Tek IIカバーグラスチェンバー(Nalgen Nunc社)にまき、37℃、5%CO<sub>2</sub>条件下で一晩培養した後、トランスフェクションした。トランスフェクションにはLipofectamine™ 2000 試薬(GIBCO BRL社)を用いた。まずLipofectamine™ 2000 試薬 3.3μlとOPTI-ME  
20 M-I(GIBCO BRL社)80μlを混合し、5分間放置後、これを0.72μgのDNAとOPTI-MEM-I 80μlの混合液と混ぜ合わせ、20分間室温で静置することによりDNAとリポフェクトアミンの複合体を形成させた。この混合液を上記のRINm5F細胞を培養したチェンバーに160μl添加し、さらに37℃、5%CO<sub>2</sub>条件下で一晩培養した。共焦点顕微鏡での観  
25 察は実施例1と同様の方法で行った。

その結果PTH-GFP融合タンパク質の細胞膜での発現が観察された。

実施例3 インスリンIIプロモーターを用いたGPCRとGFP融合タンパク質の発現

実施例1と同様の方法で、マウスゲノムからクローニングしたマウスインスリンIIプロモーターの下流に、ヒトGPR40（配列番号：15）のC末端にGFPをつないだ断片を挿入し、GPR40とGFPとの融合タンパク質（以下、GPR40-GFP）を発現させるための発現ベクターを作製した。このようにして得たGPR40-GFPの発現ベクタープラスミドを以下の方法でMIN6細胞にトランスフェクションした。MIN6細胞は増殖培地 [DMEM (4.5 g / l Glucose含有) (Invitrogen社) に最終濃度ウシ胎児血清 (Trace社) を15%、55  $\mu$ M 2-mercaptoethanol (Invitrogen社)、20mM HEPES (大日本製薬 社) をそれぞれ添加したもの] に懸濁し、 $1.2 \times 10^5$  cells / チャンバーの濃度にてチェンバー数4つのLab Tek IIカバーグラスチェンバー (Nalge Nunc社) にまき、37℃、5% CO<sub>2</sub>条件下で二晩培養した後にトランスフェクションした。トランスフェクションにはLipofectamine™ 2000 試薬 (Invitrogen社) を用いた。まずLipofectamine™ 2000 試薬4  $\mu$ lとOpti-MEM培地 (Invitrogen社) 100  $\mu$ lを混合し、5分間放置後、これを2  $\mu$ gのDNAとOpti-MEM培地100  $\mu$ lの混合液と混ぜ合わせ、20分間室温で静置することによりDNAとリポフェクトアミンの複合体を形成させた。この混合液を上記のMIN6細胞を培養したチェンバーに100  $\mu$ l添加し、37℃、5% CO<sub>2</sub>条件下で4時間培養後、新たな増殖培地400  $\mu$ lに交換し、さらに一晩培養した。共焦点顕微鏡での観察は実施例1と同様の方法で行った。

その結果、GPR40-GFP融合タンパク質がMIN6細胞の細胞膜で発現しているのが観察された。

#### 25 実施例4 102種類の融合タンパク質をそれぞれ発現し得る形質転換体の製造

実施例1の方法に準じて、リガンドが決定されていない102種類の各レセプタータンパク質と配列番号：1で表されるアミノ酸配列またはその改変アミノ酸配列からなるGFPとの融合タンパク質をコードするDNA（配列番号132～配列番号：233）をそれぞれ含有する102種類の発現ベクタープラスミドを

調製し、CHO-mock細胞にトランスフェクションした。これらのCHO細胞を実施例1と同様に培養したところ、融合タンパク質の発現がCHO-mock細胞に観察された。

#### 5 産業上の利用可能性

本発明の、リガンドが決定されていないレセプタータンパク質のリガンドの決定方法は、各種の細胞系を使用できるため簡便であり、かつ短時間で実施することができる。

## 請求の範囲

1. リガンドが決定されていないレセプタータンパク質と蛍光タンパク質との融合タンパク質を用いることを特徴とする該レセプタータンパク質に対するリガンドの決定方法。
- 5 2. リガンドが決定されていないレセプタータンパク質とGFPとの融合タンパク質を用いることを特徴とする請求項1記載のリガンドの決定方法。
3. リガンドが決定されていないレセプタータンパク質とGFPとの融合タンパク質を発現している細胞またはその細胞膜画分と、試験化合物とを接触させることを特徴とする請求項1記載のリガンドの決定方法。
- 10 4. (1) アラキドン酸遊離、アセチルコリン遊離、細胞内Ca<sup>2+</sup>遊離、細胞内cAMP生成、細胞内cGMP生成、イノシトールリン酸産生、細胞膜電位変動、細胞内タンパク質のリン酸化、c-fos活性化またはpHの低下を促進する活性または抑制する活性、(2) MAPキナーゼの活性化、(3) 転写因子の活性化、(4) ジアシルグリセロール産生、(5) 細胞膜上のイオンチャネルの開閉、(6) アポトーシスの誘導、(7) 形態変化、(8) 該融合タンパク質の細胞膜から細胞質への移行、(9) 低分子量Gタンパク質の活性化、(10) 細胞分裂促進活性または(11) DNA合成促進活性を測定することを特徴とする請求項1記載のリガンドの決定方法。
- 15 5. 該融合タンパク質の細胞膜から細胞質への移行を測定することを特徴とする請求項1記載のリガンドの決定方法。
6. GFP蛍光を観察することにより該融合タンパク質の細胞膜から細胞質への移行を測定する請求項5記載のリガンドの決定方法。
7. リガンドが決定されていないレセプタータンパク質と蛍光タンパク質との融合タンパク質を発現し、かつ、cAMPレスポンスエレメント/プロモーターの下流にレポータータンパク質をコードするDNAを連結したプラスミドを含有する細胞と試験化合物とを接触させて、レポータータンパク質の活性を測定することを特徴とする請求項1記載のリガンドの決定方法。
- 25 8. (1) リガンドが決定されていないレセプタータンパク質と蛍光タンパク質との融合タンパク質をコードするDNAを含有するプラスミドおよび(2) cA

MPレスポンスエレメント／プロモーターの下流にレポータータンパク質をコードするDNAを連結したプラスミドを含有する細胞を培養し、試験化合物と接触させてレポータータンパク質の活性を測定することを特徴とする請求項7記載の方法。

- 5 9. リガンドが決定されていないレセプタータンパク質とGFPとの融合タンパク質を発現し、かつ、cAMPレスポンスエレメント／プロモーターの下流にレポータータンパク質をコードするDNAを連結したプラスミドを含有する細胞と試験化合物とを接触させて、レポータータンパク質の活性を測定することを特徴とする請求項2記載のリガンドの決定方法。
- 10 10. (1) リガンドが決定されていないレセプタータンパク質とGFPとの融合タンパク質をコードするDNAを含有するプラスミドおよび(2) cAMPレスポンスエレメント／プロモーターの下流にレポータータンパク質をコードするDNAを連結したプラスミドを含有する細胞を培養し、試験化合物と接触させてレポータータンパク質の活性を測定することを特徴とする請求項9記載の方法。
- 15 11. レセプタータンパク質がGタンパク質共役型レセプタータンパク質である請求項1記載の方法。  
12. GFPが配列番号：1、配列番号：3、配列番号：5または配列番号：7で表わされるアミノ酸配列と同一または実質的に同一のアミノ酸配列を含有するタンパク質である請求項1記載の方法。
- 20 13. プロモーターがTATA様配列である請求項7記載の方法。  
14. レポータータンパク質がルシフェラーゼである請求項7記載の方法。  
15. プラスミドがcAMPレスポンスエレメントの下流にTATA様プロモーターおよびレポータータンパク質をコードする遺伝子を連結したものである請求項7記載の方法。
- 25 16. 細胞が、リガンドが決定されていない2種類以上のレセプタータンパク質を発現している請求項7記載の方法。  
17. 細胞が、抑制性Gタンパク質 $\alpha$ サブユニットGiをコードする遺伝子を含有するプラスミドを更に含有する請求項7記載の方法。  
18. さらにフォルスコリンを添加する請求項7記載の方法。

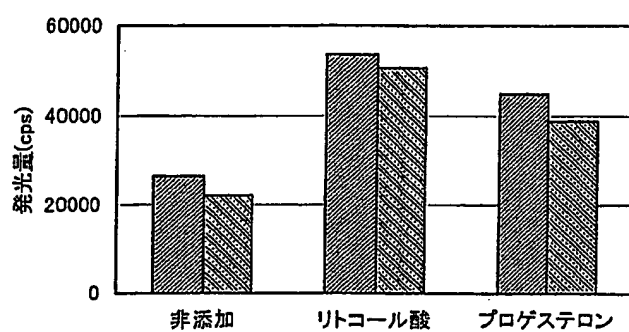
19. 2種類以上のレセプタータンパク質が類似の特徴を有することを特徴とする請求項16記載の方法。
20. 類似の特徴がレポータータンパク質の基礎発現量および（または）フォルスコリン添加時のレポータータンパク質の発現量である請求項19記載の方法。
- 5 21. 予め2種類以上のレセプタータンパク質をそれぞれ単独で発現させた時のレポータータンパク質の基礎発現量および／またはフォルスコリン添加時のレポータータンパク質の発現量を測定し、該レポータータンパク質の発現量が同程度である2種類以上のレセプタータンパク質を組み合わせ発現させることを特徴とする請求項16記載の方法。
- 10 22. リガンドが決定されていないレセプタータンパク質と蛍光タンパク質との融合タンパク質またはその塩。
23. 蛍光タンパク質がGFPである請求項22記載の融合タンパク質またはその塩。
24. 請求項22記載の融合タンパク質をコードするDNAを含有するDNA。
- 15 25. 請求項24記載のDNAを含有する組換えベクター。
26. 請求項25記載の組換えベクターで形質転換させた形質転換体。
27. リガンドが決定されていないレセプタータンパク質に対するリガンドを決定するための蛍光タンパク質の使用。
28. リガンドが決定されていないレセプタータンパク質に対するリガンドを決定するためのGFPの使用。
- 20



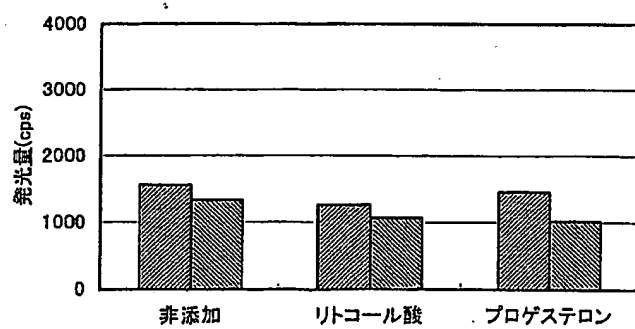
1/5

図 1

A

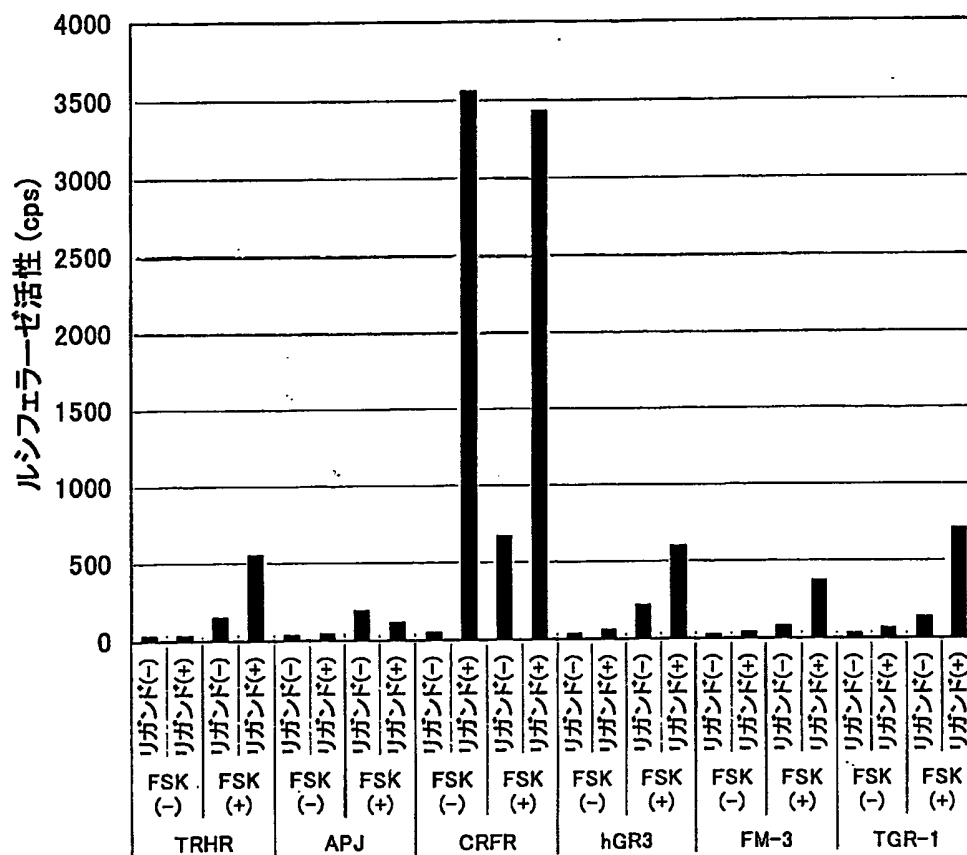


B



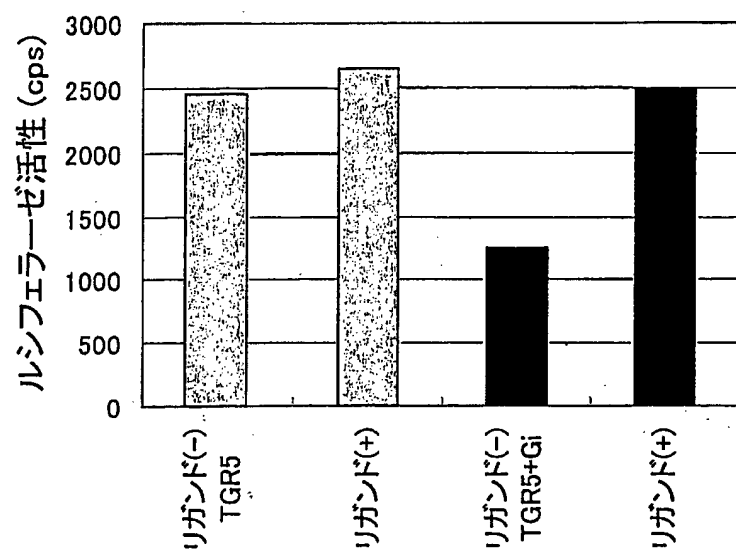
2/5

図 2



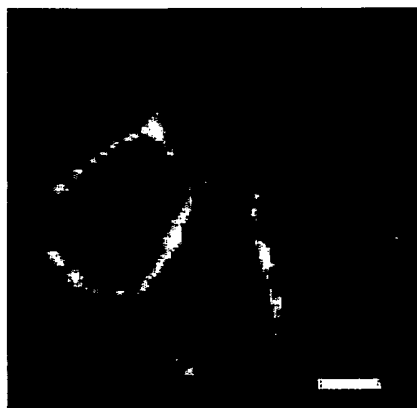
3/5

図 3



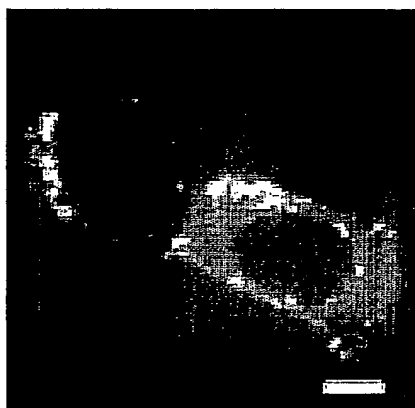
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図 4



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図 5



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SEQUENCE LISTING

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<150> JP 2002-213949

<151> 2002-07-23

<150> JP 2002-298237

<151> 2002-10-11

<160> 233

<210> 1

<211> 239

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant of wild-type GFP

<400> 1

Met Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu

2/518

	5	10	15
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly			
	20	25	30
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile			
	35	40	45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr			
	50	55	60
Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys			
	65	70	75
Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu			
	85	90	95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu			
	100	105	110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly			
	115	120	125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr			
	130	135	140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn			
	145	150	155
Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser			
	165	170	175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly			
	180	185	190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu			
	195	200	205
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe			
	210	215	220
Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn			
	225	230	235

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&lt;210&gt; 2

&lt;211&gt; 717

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Variant of wild-type GFP cDNA

&lt;400&gt; 2

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atggctagca aaggagaaga actcttcact ggagttgtcc caattcttgt tgaattagat    60
ggtgatgita acggccacaa gttctctgtc agtggagagg gtgaaggta tgcaacatac   120
ggaaaactta cctgaagtt catctgcact actggcaaac tgcctgttcc atggccaaca   180
ctagtcacta ctctgtgcta tggigttaa tgcttttcaa gatacccgga tcatatgaaa   240
cggcatgact ttttcaagag tgccatgccc gaaggttatg tacaggaaag gaccatcttc   300
ttcaaagatg acggcaacta caagacacgt gctgaagtca agtttgaagg tgataccctt   360
gttaatagaa tcgagttaaa aggtattgac ttcaaggaag atggcaacat tctgggacac   420
aaattggaat acaactataa ctacacaaat gtatacatca tggcagacaa acaaaagaat   480
ggaatcaaag tgaacttcaa gaccgcccac aacattgaag atggaagcgt tcaactagca   540
gaccattatc aacaaaatac tccaattggc gatggccctg tccttttacc agacaacat    600
tacctgtcca cacaatctgc cttttcgaaa gatcccaacg aaaagagaga ccacatggtc   660
cttcttgagt ttgtaacagc tgctgggatt acacatggca tggatgaact gtacaac     717
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&lt;210&gt; 3

&lt;211&gt; 238

&lt;212&gt; PRT

<213> *Aequorea coerulescens*

&lt;400&gt; 3



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Met Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val  
                   5                          10                          15  
 Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu  
                   20                          25                          30  
 Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys  
                   35                          40                          45  
 Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Phe  
                   50                          55                          60  
 Ser Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg  
                   65                          70                          75                          80  
 His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg  
                   85                          90                          95  
 Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val  
                   100                          105                          110  
 Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile  
                   115                          120                          125  
 Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn  
                   130                          135                          140  
 Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly  
                   145                          150                          155                          160  
 Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val  
                   165                          170                          175  
 Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro  
                   180                          185                          190  
 Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser  
                   195                          200                          205  
 Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val  
                   210                          215                          220  
 Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Lys

5/518

225

230

235

&lt;210&gt; 4

&lt;211&gt; 714

&lt;212&gt; DNA

<213> *Aequorea coerulescens*

&lt;400&gt; 4

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atgagtaaag gagaagaact ttctactgga gtigtcccaa ttcttgttga attagatggt    60
gatgttaatg ggcacaaatt ttctgtcagt ggagagggig aaggtgatgc aacatacgga    120
aaacttacc ttaaatttat ttgcactact ggaaaactac ctgttccatg gccaacactt    180
gtcactactt tctcttatgg tgttcaatgc ttttcaagat acccagatca tatgaaacgg    240
catgactttt tcaagagtgc catgcccga ggttatgtac aggaaagaac tatatttttc    300
aaagatgacg ggaactacaa gacacgtgct gaagtcaagt ttgaaggatg tacccttggt    360
aatagaatcg agttaaaagg tattgatatt aaagaagatg gaaacattct tggacacaaa    420
ttggaataca actataactc acacaatgta tacatcatgg cagacaaaca aaagaatgga    480
atcaaagtta acttcaaaat tagacacaac attgaagatg gaagcgttca actagcagac    540
cattatcaac aaaatactcc aatiggcgtg ggccctgtcc ttttaccaga caaccattac    600
ctgtccacac aatctgccct ttcgaaagat cccaacgaaa agagagacca catggtcctt    660
cttgagtttg taacagctgc tgggattaca catggcatgg atgaactata caaa          714

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&lt;210&gt; 5

&lt;211&gt; 238

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Variant of wild-type GFP

6/518

&lt;400&gt; 5

Met Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val  
5 10 15  
Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu  
20 25 30  
Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys  
35 40 45  
Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Phe  
50 55 60  
Ser Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg  
65 70 75 80  
His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg  
85 90 95  
Thr Ile Ser Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val  
100 105 110  
Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile  
115 120 125  
Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn  
130 135 140  
Tyr Asn Ser His Asn Val Tyr Ile Thr Ala Asp Lys Gln Lys Asn Gly  
145 150 155 160  
Ile Lys Ala Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser Val  
165 170 175  
Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro  
180 185 190  
Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser  
195 200 205  
Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val  
210 215 220

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Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Lys

225

230

235

&lt;210&gt; 6

&lt;211&gt; 714

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Variant of wild-type GFP cDNA

&lt;400&gt; 6

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atgagtaaag gagaagaact ttctactgga gttgtcccaa ttcttggtga attagatggt    60
gatgttaatg ggcacaaatt ttctgtcagt ggagagggtg aaggatgatc aacatacggg    120
aaacttaccc ttaaatttat ttgcactact ggaaaactac ctgttccatg gccaacactt    180
gtcactactt tctcttatgg tgttcaatgc ttttccggtt atccggatca tatgaaacgg    240
catgactttt tcaagagtgc catgcccga ggttatgtac aggaacgcac tatatctttc    300
aaagatgacg ggaactacaa gacgcgtgct gaagtcaagt ttgaaggatg tacccttggt    360
aatcgtatcg agttaaaggg tattgatttt aaagaagatg gaaacattct cggacacaaa    420
ctcgagtaca actataactc acacaatgta tacatcacgg cagacaaaca aaagaatgga    480
atcaaagcta acttcaaaat tcgccacaac attgaagatg gatccgttca actagcagac    540
cattatcaac aaaatactcc aattggcgat ggccctgtcc ttttaccaga caaccattac    600
ctgtcgacac aatctgccct ttcgaaagat cccaacgaaa agcgtgacca catggtcctt    660
cttgagtttg taactgctgc tgggattaca catggcatgg atgagctcta caaa          714

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&lt;210&gt; 7

&lt;211&gt; 239

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

8/518

&lt;220&gt;

&lt;223&gt; Variant of wild-type GFP

&lt;400&gt; 7

Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu  
                     5                    10                    15  
 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly  
                     20                    25                    30  
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile  
                     35                    40                    45  
 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr  
                     50                    55                    60  
 Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys  
                     65                    70                    75                    80  
 Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu  
                     85                    90                    95  
 Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu  
                     100                    105                    110  
 Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly  
                     115                    120                    125  
 Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr  
                     130                    135                    140  
 Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn  
                     145                    150                    155                    160  
 Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser  
                     165                    170                    175  
 Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly  
                     180                    185                    190

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Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu  
                   195                  200                  205  
 Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe  
                   210                  215                  220  
 Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys  
                   225                  230                  235

&lt;210&gt; 8

&lt;211&gt; 717

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Variant of wild-type GFP cDNA

&lt;400&gt; 8

```

atggtgagca agggcgagga gctgttcacc ggggtggtgc ccatcctggt cgagctggac   60
ggcgacgtaa acggccacaa gttcagcgtg tccggcgagg gcgagggcga tgccacctac   120
ggcaagctga ccctgaagtt catctgcacc accggcaagc tgcccgtgcc ctggcccacc   180
ctcgtgacca ccctgacctg cggcgtgcag tgcttcagcc gctaccccga ccacatgaag   240
cagcacgact tcttcaagtc cgccatgccc gaaggctacg tccaggagcg caccatcttc   300
ttcaaggacg acggcaacta caagacccgc gccgaggtga agttcgaggg cgacaccctg   360
gtgaaccgca tcgagctgaa gggcatcgac ttcaaggagg acggcaacat cctggggcac   420
aagctggagt acaactacaa cagccacaac gtctatatca tggccgacaa gcagaagaac   480
ggcatcaagg tgaacttcaa gatccgccac aacatcgagg acggcagcgt gcagctcgcc   540
gaccactacc agcagaacac ccccatcggc gacggccccg tgcgtgctgcc cgacaaccac   600
tacctgagca cccagtcgcg cctgagcaaa gaccccaacg agaagcgcga tcacatggtc   660
ctgctggagi tcgtgaccgc cgccgggatc actctcggca tggacgagct gtacaag    717

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&lt;210&gt; 9

&lt;211&gt; 330

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 9

Met Thr Pro Asn Ser Thr Gly Glu Val Pro Ser Pro Ile Pro Lys Gly  
                             5                            10                            15  
 Ala Leu Gly Leu Ser Leu Ala Leu Ala Ser Leu Ile Ile Thr Ala Asn  
                             20                            25                            30  
 Leu Leu Leu Ala Leu Gly Ile Ala Trp Asp Arg Arg Leu Arg Ser Pro  
                             35                            40                            45  
 Pro Ala Gly Cys Phe Phe Leu Ser Leu Leu Leu Ala Gly Leu Leu Thr  
                             50                            55                            60  
 Gly Leu Ala Leu Pro Thr Leu Pro Gly Leu Trp Asn Gln Ser Arg Arg  
                             65                            70                            75                            80  
 Gly Tyr Trp Ser Cys Leu Leu Val Tyr Leu Ala Pro Asn Phe Ser Phe  
                             85                            90                            95  
 Leu Ser Leu Leu Ala Asn Leu Leu Leu Val His Gly Glu Arg Tyr Met  
                             100                            105                            110  
 Ala Val Leu Arg Pro Leu Gln Pro Pro Gly Ser Ile Arg Leu Ala Leu  
                             115                            120                            125  
 Leu Leu Thr Trp Ala Gly Pro Leu Leu Phe Ala Ser Leu Pro Ala Leu  
                             130                            135                            140  
 Gly Trp Asn His Trp Thr Pro Gly Ala Asn Cys Ser Ser Gln Ala Ile  
                             145                            150                            155                            160  
 Phe Pro Ala Pro Tyr Leu Tyr Leu Glu Val Tyr Gly Leu Leu Leu Pro  
                             165                            170                            175  
 Ala Val Gly Ala Ala Ala Phe Leu Ser Val Arg Val Leu Ala Thr Ala

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	180		185		190										
His	Arg	Gln	Leu	Gln	Asp	Ile	Cys	Arg	Leu	Glu	Arg	Ala	Val	Cys	Arg
	195		200		205										
Asp	Glu	Pro	Ser	Ala	Leu	Ala	Arg	Ala	Leu	Thr	Trp	Arg	Gln	Ala	Arg
	210		215		220										
Ala	Gln	Ala	Gly	Ala	Met	Leu	Leu	Phe	Gly	Leu	Cys	Trp	Gly	Pro	Tyr
225			230		235				240						
Val	Ala	Thr	Leu	Leu	Leu	Ser	Val	Leu	Ala	Tyr	Glu	Gln	Arg	Pro	Pro
	245		250		255										
Leu	Gly	Pro	Gly	Thr	Leu	Leu	Ser	Leu	Leu	Ser	Leu	Gly	Ser	Ala	Ser
	260		265		270										
Ala	Ala	Ala	Val	Pro	Val	Ala	Met	Gly	Leu	Gly	Asp	Gln	Arg	Tyr	Thr
	275		280		285										
Ala	Pro	Tyr	Arg	Ala	Ala	Ala	Gln	Arg	Cys	Leu	Gln	Gly	Leu	Trp	Gly
	290		295		300										
Arg	Ala	Ser	Arg	Asp	Ser	Pro	Gly	Pro	Ser	Ile	Ala	Tyr	His	Pro	Ser
305			310		315				320						
Ser	Gln	Ser	Ser	Val	Asp	Leu	Asp	Leu	Asn						
	325		330												

&lt;210&gt; 10

&lt;211&gt; 990

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 10

atgacgccca	acagcactgg	cgagggtccc	agccccattc	ccaagggggc	tttggggctc	60
tccctggccc	tggcaagcct	catcatcacc	gcgaacctgc	tcctagccct	gggcatcgcc	120
tgggaccgcc	gcctgcgcag	cccacctgct	ggctgcttct	tcctgagcct	actgctggct	180



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gggctgctca cgggtctggc attgcccaca ttgccagggc tgtggaacca gagtcgccgg 240
ggttactggg cctgcctcct cgtctacttg gctcccaact tctccttctt ctccttgctt 300
gccaacctct tgctggtgca cggggagcgc tacatggcag tcctgaggcc actccagccc 360
cctgggagca ttcggctggc cctgctcctc acctgggctg gtcccttctt ctttgccagt 420
ctgcccgctc tggggtggaa ccactggacc cctggtgcca actgcagctc ccaggctatc 480
ttcccagccc cctacctgta cctcgaagtc tatgggctcc tgctgccgcg cgtgggtgct 540
gctgccttcc tctctgtccg cgtgtggcc actgcccacc gccagctgca ggacatctgc 600
cggctggagc gggcagtggt ccgcgatgag cctccgccc tggcccgggc cttacctgg 660
aggcaggcaa gggcacaggc tggagccatg ctgctcttcg ggctgtgctg ggggccctac 720
gtggccacac tgctcctctc agtcttggcc tatgagcagc gcccgccact ggggcctggg 780
acactgttgt cctcctctc cctaggaagt gccagtgcag cggcagtgcc cgtagccatg 840
gggctgggcg atcagcgcta cacagcccc tggagggcag ccgccc aaag gtgcctgcag 900
gggctgtggg gaagagcctc ccgggacagt cccggcccca gcattgccta ccaccaagc 960
agccaaagca gtgtcgacct ggacttgaac 990

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&lt;210&gt; 11

&lt;211&gt; 30

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Designed oligonucleotide primer to amplify DNA encoding TGR5

&lt;400&gt; 11

gatgacgccc aacagcactg gcgaggtgcc 30

&lt;210&gt; 12

&lt;211&gt; 31

&lt;212&gt; DNA

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&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Designed oligonucleotide primer to amplify DNA encoding TGR5

&lt;400&gt; 12

ttagttcaag tccaggtcga cactgctttg g 31

&lt;210&gt; 13

&lt;211&gt; 593

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 13

Met	Gly	Thr	Ala	Arg	Ile	Ala	Pro	Gly	Leu	Ala	Leu	Leu	Leu	Cys	Cys	
				5				10					15			
Pro	Val	Leu	Ser	Ser	Ala	Tyr	Ala	Leu	Val	Asp	Ala	Asp	Asp	Val	Met	
				20				25					30			
Thr	Lys	Glu	Glu	Gln	Ile	Phe	Leu	Leu	His	Arg	Ala	Gln	Ala	Gln	Cys	
				35				40					45			
Glu	Lys	Arg	Leu	Lys	Glu	Val	Leu	Gln	Arg	Pro	Ala	Ser	Ile	Met	Glu	
				50				55					60			
Ser	Asp	Lys	Gly	Trp	Thr	Ser	Ala	Ser	Thr	Ser	Gly	Lys	Pro	Arg	Lys	
				65				70					75		80	
Asp	Lys	Ala	Ser	Gly	Lys	Leu	Tyr	Pro	Glu	Ser	Glu	Glu	Asp	Lys	Glu	
				85				90					95			
Ala	Pro	Thr	Gly	Ser	Arg	Tyr	Arg	Gly	Arg	Pro	Cys	Leu	Pro	Glu	Trp	
				100				105					110			
Asp	His	Ile	Leu	Cys	Trp	Pro	Leu	Gly	Ala	Pro	Gly	Glu	Val	Val	Ala	

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115	120	125
Val Pro Cys Pro Asp Tyr Ile Tyr Asp Phe Asn His Lys Gly His Ala		
130	135	140
Tyr Arg Arg Cys Asp Arg Asn Gly Ser Trp Glu Leu Val Pro Gly His		
145	150	155
Asn Arg Thr Trp Ala Asn Tyr Ser Glu Cys Val Lys Phe Leu Thr Asn		
165	170	175
Glu Thr Arg Glu Arg Glu Val Phe Asp Arg Leu Gly Met Ile Tyr Thr		
180	185	190
Val Gly Tyr Ser Val Ser Leu Ala Ser Leu Thr Val Ala Val Leu Ile		
195	200	205
Leu Ala Tyr Phe Arg Arg Leu His Cys Thr Arg Asn Tyr Ile His Met		
210	215	220
His Leu Phe Leu Ser Phe Met Leu Arg Ala Val Ser Ile Phe Val Lys		
225	230	235
Asp Ala Val Leu Tyr Ser Gly Ala Thr Leu Asp Glu Ala Glu Arg Leu		
245	250	255
Thr Glu Glu Glu Leu Arg Ala Ile Ala Gln Ala Pro Pro Pro Pro Ala		
260	265	270
Thr Ala Ala Ala Gly Tyr Ala Gly Cys Arg Val Ala Val Thr Phe Phe		
275	280	285
Leu Tyr Phe Leu Ala Thr Asn Tyr Tyr Trp Ile Leu Val Glu Gly Leu		
290	295	300
Tyr Leu His Ser Leu Ile Phe Met Ala Phe Phe Ser Glu Lys Lys Tyr		
305	310	315
Leu Trp Gly Phe Thr Val Phe Gly Trp Gly Leu Pro Ala Val Phe Val		
325	330	335
Ala Val Trp Val Ser Val Arg Ala Thr Leu Ala Asn Thr Gly Cys Trp		
340	345	350

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Asp Leu Ser Ser Gly Asn Lys Lys Trp Ile Ile Gln Val Pro Ile Leu  
 355 360 365  
 Ala Ser Ile Val Leu Asn Phe Ile Leu Phe Ile Asn Ile Val Arg Val  
 370 375 380  
 Leu Ala Thr Lys Leu Arg Glu Thr Asn Ala Gly Arg Cys Asp Thr Arg  
 385 390 395 400  
 Gln Gln Tyr Arg Lys Leu Leu Lys Ser Thr Leu Val Leu Met Pro Leu  
 405 410 415  
 Phe Gly Val His Tyr Ile Val Phe Met Ala Thr Pro Tyr Thr Glu Val  
 420 425 430  
 Ser Gly Thr Leu Trp Gln Val Gln Met His Tyr Glu Met Leu Phe Asn  
 435 440 445  
 Ser Phe Gln Gly Phe Phe Val Ala Ile Ile Tyr Cys Phe Cys Asn Gly  
 450 455 460  
 Glu Val Gln Ala Glu Ile Lys Lys Ser Trp Ser Arg Trp Thr Leu Ala  
 465 470 475 480  
 Leu Asp Phe Lys Arg Lys Ala Arg Ser Gly Ser Ser Ser Tyr Ser Tyr  
 485 490 495  
 Gly Pro Met Val Ser His Thr Ser Val Thr Asn Val Gly Pro Arg Val  
 500 505 510  
 Gly Leu Gly Leu Pro Leu Ser Pro Arg Leu Leu Pro Thr Ala Thr Thr  
 515 520 525  
 Asn Gly His Pro Gln Leu Pro Gly His Ala Lys Pro Gly Thr Pro Ala  
 530 535 540  
 Leu Glu Thr Leu Glu Thr Thr Pro Pro Ala Met Ala Ala Pro Lys Asp  
 545 550 555 560  
 Asp Gly Phe Leu Asn Gly Ser Cys Ser Gly Leu Asp Glu Glu Ala Ser  
 565 570 575  
 Gly Pro Glu Arg Pro Pro Ala Leu Leu Gln Glu Glu Trp Glu Thr Val

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580

585

590

Met

&lt;210&gt; 14

&lt;211&gt; 1779

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 14

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atggggaccg cccggatcgc acccggcctg gcgctcctgc tctgctgcc cgtgctcagc   60
tccgcgtacg cgctgggtga tgcagatgac gtcatgacta aagaggaaca gatcttccig  120
ctgcaccgtg ctccaggcca gtgcgaaaaa cggctcaagg aggtcctgca gaggccagcc  180
agcataatgg aatcagacaa gggatggaca tctgcgtcca catcaggga gcccaggaaa  240
gataaggcat ctgggaagct ctacctgag tctgaggagg acaaggaggc acccactggc  300
agcaggtacc gagggcgccc ctgtctgcc gaatgggacc acatcctgtg ctggccgctg  360
ggggcaccag gtgaggtggt ggctgtgcc tgtccgact acatttatga cttcaatcac  420
aaaggccatg cctaccgacg ctgtgaccgc aatggcagct gggagctggt gcctgggcac  480
aacaggacgt gggccaacta cagcgagtgt gtcaaatttc tcaccaatga gactcgtgaa  540
cgggaggtgt ttgaccgcct gggcatgatt tacaccgtgg gctactccgt gtccttgccg  600
tccctcaccg tagctgtgct catcctggcc tactttaggc ggctgcactg cacgcgcaac  660
tacatccaca tgcacctggt cctgtccttc atgtgcgcg ccgtgagcat cttcgtcaag  720
gacgctgtgc tctactctgg cgccacgctt gatgaggctg agcgccctac cgaggaggag  780
ctgcgcgcca tcgccaggc gccccgccg cctgccaccg ccgtgccgg ctacgcgggc  840
tgcagggtgg ctgtgacctt cttcctttac ttctggcca ccaactacta ctggattctg  900
gtggaggggc tgtacctgca cagcctcatc ttcatggcct tcttctcaga gaagaagtac  960
ctgtggggct tcacagtctt cggctggggt ctgccgctg tcttcgtggc tgtgtgggtc 1020
agtgtcagag ctacctggc caacaccggg tgctgggact tgagctccgg gaacaaaaag 1080
tggatcatcc agtgcccat cctggcctcc attgtgctca acttcatcct cttcatcaat 1140
atcgtccggg tgctcgccac caagctgcgg gagaccaacg ccggccggtg tgacacacgg 1200

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17/518

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cagcagtacc ggaagctgct caaatccacg ctggtgctca tgccctctt tggcgctccac 1260
tacattgtct tcatggccac accatacacc gaggctcag ggacgctctg gcaagtcag 1320
atgcactatg agatgctctt caactccttc cagggaattt ttgtcgcaat catatactgt 1380
ttctgcaatg gcgaggtaca agctgagatc aagaaatctt ggagccgctg gacactggca 1440
ctggacttca agcgaaaggc acgcagcggg agcagcagct atagctacgg ccccatgggtg 1500
tcccacacaa gtgtgaccaa tgtcggcccc cgtgtgggac tcggcctgcc cctcagcccc 1560
cgcctactgc ccactgccac caccaacggc caccctcagc tgccctggcca tgccaagcca 1620
gggaccccag ccttgagac cctcgagacc acaccacctg ccatggctgc tcccaaggac 1680
gatgggttcc tcaacggctc ctgctcaggc ctggacgagg aggcctctgg gcctgagcgg 1740
ccacctgccc tgctacagga agagtgggag acagtcatg 1779

```

&lt;210&gt; 15

&lt;211&gt; 300

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 15

Met Asp Leu Pro Pro Gln Leu Ser Phe Gly Leu Tyr Val Ala Ala Phe

5

10

15

Ala Leu Gly Phe Pro Leu Asn Val Leu Ala Ile Arg Gly Ala Thr Ala

20

25

30

His Ala Arg Leu Arg Leu Thr Pro Ser Leu Val Tyr Ala Leu Asn Leu

35

40

45

Gly Cys Ser Asp Leu Leu Leu Thr Val Ser Leu Pro Leu Lys Ala Val

50

55

60

Glu Ala Leu Ala Ser Gly Ala Trp Pro Leu Pro Ala Ser Leu Cys Pro

65

70

75

80

Val Phe Ala Val Ala His Phe Phe Pro Leu Tyr Ala Gly Gly Gly Phe

85

90

95

18/518

Leu Ala Ala Leu Ser Ala Gly Arg Tyr Leu Gly Ala Ala Phe Pro Leu  
                   100                  105                  110  
 Gly Tyr Gln Ala Phe Arg Arg Pro Cys Tyr Ser Trp Gly Val Cys Ala  
                   115                  120                  125  
 Ala Ile Trp Ala Leu Val Leu Cys His Leu Gly Leu Val Phe Gly Leu  
                   130                  135                  140  
 Glu Ala Pro Gly Gly Trp Leu Asp His Ser Asn Thr Ser Leu Gly Ile  
 145                  150                  155                  160  
 Asn Thr Pro Val Asn Gly Ser Pro Val Cys Leu Glu Ala Trp Asp Pro  
                   165                  170                  175  
 Ala Ser Ala Gly Pro Ala Arg Phe Ser Leu Ser Leu Leu Leu Phe Phe  
                   180                  185                  190  
 Leu Pro Leu Ala Ile Thr Ala Phe Cys Tyr Val Gly Cys Leu Arg Ala  
                   195                  200                  205  
 Leu Ala Arg Ser Gly Leu Thr His Arg Arg Lys Leu Arg Ala Ala Trp  
                   210                  215                  220  
 Val Ala Gly Gly Ala Leu Leu Thr Leu Leu Leu Cys Val Gly Pro Tyr  
 225                  230                  235                  240  
 Asn Ala Ser Asn Val Ala Ser Phe Leu Tyr Pro Asn Leu Gly Gly Ser  
                   245                  250                  255  
 Trp Arg Lys Leu Gly Leu Ile Thr Gly Ala Trp Ser Val Val Leu Asn  
                   260                  265                  270  
 Pro Leu Val Thr Gly Tyr Leu Gly Arg Gly Pro Gly Leu Lys Thr Val  
                   275                  280                  285  
 Cys Ala Ala Arg Thr Gln Gly Gly Lys Ser Gln Lys  
                   290                  295                  300

&lt;210&gt; 16

&lt;211&gt; 900

19/518

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 16

```
atggacctgc ccccgagct ctccctcggc ctctatgtgg ccgcccttgc gctgggcctc   60
ccgctcaacg tccctggccat ccgaggcgcg acggcccacg cccggctccg tctcaccctt  120
agcctggict acgccctgaa cctgggctgc tccgacctgc tgcagacagt ctctctgccc  180
ctgaaggcgg tggaggcgct agcctccggg gccctggcctc tgcgggcctc gctgtgcccc  240
gtcttcgcgg tggcccactt cttcccactc tatgccggcg ggggcttctt ggccgcccctg  300
agtgcaggcc gctacctggg agcagccttc ccttgggct accaagcctt ccggaggccg  360
tgctattcct ggggggtgtg cgcggccatc tgggcccctg tccgtgtca cctgggtctg  420
gtctttgggt tggaggctcc aggaggctgg ctggaccaca gcaacacctc cctgggcctc  480
aacacaccgg tcaacggctc tccggtctgc ctggaggcct gggaccgggc ctctgccggc  540
ccggcccgtt tcagcctctc tctcctgctc tttttctgc ccttggccat cacagccttc  600
tgctacgtgg gctgccctcg ggcactggcc cgctccggcc tgacgcacag gcggaagctg  660
cgggccgcct ggggtggccgg cggggccctc ctacagctgc tgctctgcgt aggaccctac  720
aacgcctcca acgtggccag ctctctgtac cccaatctag gaggtcctg gcggaagctg  780
gggctcatca cgggtgcctg gagtgtgtg cttaatccgc tggtagaccg ttacttggga  840
aggggtcctg gcctgaagac agtgtgtgcg gcaagaacgc aagggggcaa gtcccagaag  900
```

&lt;210&gt; 17

&lt;211&gt; 6

&lt;212&gt; PRT

&lt;213&gt; Artificial sequence

&lt;220&gt;

&lt;223&gt; His-tag

&lt;400&gt; 17



20/518

His His His His His His

1 5

&lt;210&gt; 18

&lt;211&gt; 14

&lt;212&gt; PRT

&lt;213&gt; Artificial sequence

&lt;220&gt;

&lt;223&gt; V5-tag

&lt;400&gt; 18

Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser Thr

1 5 10

&lt;210&gt; 19

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Artificial sequence

&lt;220&gt;

&lt;223&gt; myc-tag

&lt;400&gt; 19

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu

1 5 10

&lt;210&gt; 20

&lt;211&gt; 8

21/518

&lt;212&gt; PRT

&lt;213&gt; Artificial sequence

&lt;220&gt;

&lt;223&gt; Xpress-tag

&lt;400&gt; 20

Asp Leu Tyr Asp Asp Asp Asp Lys

1 5

&lt;210&gt; 21

&lt;211&gt; 16

&lt;212&gt; PRT

&lt;213&gt; Artificial sequence

&lt;220&gt;

&lt;223&gt; HA-tag

&lt;400&gt; 21

Met Gly Ser Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Ser Leu Glu Phe

1 5 10 15

&lt;210&gt; 22

&lt;211&gt; 239

&lt;212&gt; PRT

&lt;213&gt; Artificial sequence

&lt;220&gt;

&lt;223&gt; Variant of wild-type GFP

22/518

&lt;400&gt; 22

Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu  
5 10 15  
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly  
20 25 30  
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile  
35 40 45  
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr  
50 55 60  
Leu Thr Trp Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys  
65 70 75 80  
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu  
85 90 95  
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu  
100 105 110  
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly  
115 120 125  
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr  
130 135 140  
Asn Tyr Ile Ser His Asn Val Tyr Ile Thr Ala Asp Lys Gln Lys Asn  
145 150 155 160  
Gly Ile Lys Ala Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser  
165 170 175  
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly  
180 185 190  
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu  
195 200 205  
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe

23/518

210	215	220
Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys		
225	230	235

&lt;210&gt; 23

&lt;211&gt; 720

&lt;212&gt; DNA

&lt;213&gt; Artificial sequence

&lt;220&gt;

&lt;223&gt; Variant of wild-type GFP cDNA

&lt;400&gt; 23

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atggtgagca agggcgagga gctgttcacc ggggtggtgc ccatcctggt cgagctggac   60
ggcgacglaa acggccacaa gttcagcgtg tccggcgagg gcgagggcga tgccacctac   120
ggcaagctga ccctgaagtt catctgcacc accggcaagc tggccgtgcc ctggcccacc   180
ctcgtgacca ccctgacctg gggcgtgcag tgcttcagcc gctaccccgga ccacatgaag   240
cagcagcact tcttcaagtc cgccatgccc gaaggctacg tccaggagcg caccatcttc   300
ttcaaggacg acggcaacta caagaccgcg gccgaggtga agttcgaggg cgacaccctg   360
gtgaaccgca tcgagctgaa gggcatcgac ttcaaggagg acggcaacat cctggggcac   420
aagctggagt acaactacat cagccacaac gtctatatca ccgccgacaa gcagaagaac   480
ggcatcaagg ccaacttcaa gatccgccac aacatcgagg acggcagcgt gcagctcgcc   540
gaccactacc agcagaacac ccccatcggc gacggccccg tgctgctgcc cgacaaccac   600
tacctgagca ccagtcctgc cctgagcaaa gaccccaacg agaagcgcgga tcacatggtc   660
ctgctggagt tcgtgaccgc cgccgggatc actctcggca tggacgagct gtacaagtaa   720

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&lt;210&gt; 24

&lt;211&gt; 239

&lt;212&gt; PRT

24/518

&lt;213&gt; Artificial sequence

&lt;220&gt;

&lt;223&gt; Variant of wild-type GFP

&lt;400&gt; 24

Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu

5

10

15

Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly

20

25

30

Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile

35

40

45

Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr

50

55

60

Phe Gly Tyr Gly Leu Gln Cys Phe Ala Arg Tyr Pro Asp His Met Lys

65

70

75

80

Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu

85

90

95

Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu

100

105

110

Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly

115

120

125

Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr

130

135

140

Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn

145

150

155

160

Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser

165

170

175

Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly

25/518

	180		185		190	
Pro	Val	Leu	Leu	Pro	Asp	Asn
				His	Tyr	Leu
				Ser	Tyr	Gln
				Ser	Ala	Leu
	195		200		205	
Ser	Lys	Asp	Pro	Asn	Glu	Lys
			Arg	Asp	His	Met
			Val	Leu	Leu	Glu
			Phe			
	210		215		220	
Val	Thr	Ala	Ala	Gly	Ile	Thr
			Leu	Gly	Met	Asp
			Glu	Leu	Tyr	Lys
	225		230		235	

&lt;210&gt; 25

&lt;211&gt; 720

&lt;212&gt; DNA

&lt;213&gt; Artificial sequence

&lt;220&gt;

&lt;223&gt; Variant of wild-type GFP cDNA

&lt;400&gt; 25

```

atggtgagca agggcgagga gctgttcacc ggggtggtgc ccatcctggt cgagctggac    60
ggcgacgtaa acggccacaa gttcagcgtg tccggcgagg gcgagggcga tgccacctac    120
ggcaagctga cctgaagtt catctgcacc accggcaagc tgcccgtgcc ctggcccacc    180
ctcgtgacca ccttcggcta cggcctgcag tgcttcgccc gctaccccgga ccacatgaag    240
cagcacgact tcttcaagtc cgccatgccc gaaggctacg tccaggagcg caccatcttc    300
ttcaaggacg acggcaacta caagaccgcg gccgaggtga agttcgaggg cgacaccctg    360
gtgaaccgca tcgagctgaa gggcatcgac ttcaaggagg acggcaacat cctggggcac    420
aagctggagt acaactacaa cagccacaac gctatatca tggccgacaa gcagaagaac    480
ggcatcaagg tgaacttcaa gatccgccac aacatcgagg acggcagcgt gcagctcgcc    540
gaccactacc agcagaacac ccccatcggc gacggccccg tgcctgctgcc cgacaaccac    600
tacctgagct accagtcgcg cctgagcaaa gaccccaacg agaagcgcga tcacatggtc    660
ctgctggagt tcgtgaccgc cgccgggata actctcggca tggacgagct gtacaagtaa    720

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26/518

&lt;210&gt; 26

&lt;211&gt; 225

&lt;212&gt; PRT

&lt;213&gt; Discosoma sp.

&lt;400&gt; 26

Met Arg Ser Ser Lys Asn Val Ile Lys Glu Phe Met Arg Phe Lys Val

5

10

15

Arg Met Glu Gly Thr Val Asn Gly His Glu Phe Glu Ile Glu Gly Glu

20

25

30

Gly Glu Gly Arg Pro Tyr Glu Gly His Asn Thr Val Lys Leu Lys Val

35

40

45

Thr Lys Gly Gly Pro Leu Pro Phe Ala Trp Asp Ile Leu Ser Pro Gln

50

55

60

Phe Gln Tyr Gly Ser Lys Val Tyr Val Lys His Pro Ala Asp Ile Pro

65

70

75

80

Asp Tyr Lys Lys Leu Ser Phe Pro Glu Gly Phe Lys Trp Glu Arg Val

85

90

95

Met Asn Phe Glu Asp Gly Gly Val Val Thr Val Thr Gln Asp Ser Ser

100

105

110

Leu Gln Asp Gly Cys Phe Ile Tyr Lys Val Lys Phe Ile Gly Val Asn

115

120

125

Phe Pro Ser Asp Gly Pro Val Met Gln Lys Lys Thr Met Gly Trp Glu

130

135

140

Ala Ser Thr Glu Arg Leu Tyr Pro Arg Asp Gly Val Leu Lys Gly Glu

145

150

155

160

Ile His Lys Ala Leu Lys Leu Lys Asp Gly Gly His Tyr Leu Val Glu

165

170

175

27/518

Phe Lys Ser Ile Tyr Met Ala Lys Lys Pro Val Gln Leu Pro Gly Tyr  
                   180                  185                  190  
 Tyr Tyr Val Asp Ser Lys Leu Asp Ile Thr Ser His Asn Glu Asp Tyr  
                   195                  200                  205  
 Thr Ile Val Glu Gln Tyr Glu Arg Thr Glu Gly Arg His His Leu Phe  
                   210                  215                  220  
 Leu  
 225

&lt;210&gt; 27

&lt;211&gt; 678

&lt;212&gt; DNA

&lt;213&gt; Discosoma sp.

&lt;400&gt; 27

atgaggctctt ccaagaatgt tatcaaggag ttcattgaggt ttaaggctcg catggaagga 60  
 acggctcaatg ggcacgagtt tgaaatagaa ggccaaggag aggggaggcc atacgaaggc 120  
 cacaataaccg taaagcttaa ggtaaccaag gggggacctt tgccatttgc ttgggatatt 180  
 ttgtcaccac aatttcagta tggaagcaag gtatatgtca agcaccttgc cgacatacca 240  
 gactataaaa agctgtcatt tcctgaagga tttaaatggg aaagggtcat gaactttgaa 300  
 gacggtagcg tcgttactgt aaccacagat tccagtttgc aggatggctg tttcatctac 360  
 aaggtcaagt tcattggcgt gaactttcct tccgatggac ctgttatgca aaagaagaca 420  
 atgggctggg aagccagcac tgagcgtttg tatcctcgtg atggcgtgtt gaaaggagag 480  
 attcataagg ctctgaagct gaaagacggt ggtcattacc tagttgaatt caaaagtatt 540  
 tacatggcaa agaagcctgt gcagctacca ggttactact atgttgactc caaactggat 600  
 ataacaagcc acaacgaaga ctatacaatc gttgagcagt atgaaagaac cgagggacgc 660  
 caccatctgt tccttttag 678

&lt;210&gt; 28



28/518

&lt;211&gt; 239

&lt;212&gt; PRT

&lt;213&gt; Artificial sequence

&lt;220&gt;

&lt;223&gt; Variant of wild-type GFP

&lt;400&gt; 28

Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu

5

10

15

Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly

20

25

30

Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile

35

40

45

Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr

50

55

60

Leu Thr His Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys

65

70

75

80

Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu

85

90

95

Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu

100

105

110

Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly

115

120

125

Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr

130

135

140

Asn Phe Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn

145

150

155

160

Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser

29/518

	165	170	175
Val	Gln	Leu	Ala
Asp	His	Tyr	Gln
Gln	Asn	Thr	Pro
Ile	Gly	Asp	Gly
	180	185	190
Pro	Val	Leu	Leu
Pro	Asp	Asn	His
Tyr	Leu	Ser	Thr
Gln	Ser	Ala	Leu
	195	200	205
Ser	Lys	Asp	Pro
Asn	Glu	Lys	Arg
Asp	His	Met	Val
Leu	Leu	Glu	Phe
	210	215	220
Val	Thr	Ala	Ala
Gly	Ile	Thr	Leu
Gly	Met	Asp	Glu
Leu	Tyr	Lys	
	225	230	235

&lt;210&gt; 29

&lt;211&gt; 720

&lt;212&gt; DNA

&lt;213&gt; Artificial sequence

&lt;220&gt;

&lt;223&gt; Variant of wild-type GFP cDNA

&lt;400&gt; 29

atggtgagca agggcgagga gctgttcacc ggggtggtgc ccatcciggt cgagctggac	60
ggcgacglaa acggccacaa gttcagcgtg tccggcgagg gcgagggcga tgccacctac	120
ggcaagctga ccctgaagtt catctgcacc accggcaagc tgcccgtgcc ctggcccacc	180
ctcgtgacca ccctgaccca cggcgtgcag tgcctcagcc gctaccccga ccacatgaag	240
cagcagcact tcttcaagtc cgccatgccc gaaggctacg tccaggagcg caccatcttc	300
ttcaaggacg acggcaacta caagacccgc gccgaggtga agttcgaggg cgacaccctg	360
gtgaaccgca tcgagctgaa gggcatcgac ttcaaggagg acggcaacat cctggggcac	420
aagctggagt acaacttcaa cagccacaac gtctatatca tggccgacaa gcagaagaac	480
ggcatcaagg tgaacttcaa gatccgccac aacatcgagg acggcagcgt gcagctcgcc	540
gaccactacc agcagaacac ccccatcggc gacggccccg tgctgctgcc cgacaaccac	600

30/518

tacctgagca cccagtcgc cctgagcaaa gaccccaacg agaagcgcga tcacatggtc 660  
 ctgctggagt tcgtgaccgc cgccgggatac actctcggca tggacgagct gtacaagtaa 720

&lt;210&gt; 30

&lt;211&gt; 544

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 30

Met Tyr Ser Phe Met Ala Gly Ser Ile Phe Ile Thr Ile Phe Gly Asn  
                     5                    10                    15  
 Leu Ala Met Ile Ile Ser Ile Ser Tyr Phe Lys Gln Leu His Thr Pro  
                     20                    25                    30  
 Thr Asn Phe Leu Ile Leu Ser Met Ala Ile Thr Asp Phe Leu Leu Gly  
                     35                    40                    45  
 Phe Thr Ile Met Pro Tyr Ser Met Ile Arg Ser Val Glu Asn Cys Trp  
                     50                    55                    60  
 Tyr Phe Gly Leu Thr Phe Cys Lys Ile Tyr Tyr Ser Phe Asp Leu Met  
                     65                    70                    75                    80  
 Leu Ser Ile Thr Ser Ile Phe His Leu Cys Ser Val Ala Ile Asp Arg  
                     85                    90                    95  
 Phe Tyr Ala Ile Cys Tyr Pro Leu Leu Tyr Ser Thr Lys Ile Thr Ile  
                     100                    105                    110  
 Pro Val Ile Lys Arg Leu Leu Leu Leu Cys Trp Ser Val Pro Gly Ala  
                     115                    120                    125  
 Phe Ala Phe Gly Val Val Phe Ser Glu Ala Tyr Ala Asp Gly Ile Glu  
                     130                    135                    140  
 Gly Tyr Asp Ile Leu Val Ala Cys Ser Ser Ser Cys Pro Val Met Phe  
                     145                    150                    155                    160

31/518

Asn Lys Leu Trp Gly Thr Thr Leu Phe Met Ala Gly Phe Phe Thr Pro			
165	170	175	
Gly Ser Met Met Val Gly Ile Tyr Gly Lys Ile Phe Ala Val Ser Arg			
180	185	190	
Lys His Ala His Ala Ile Asn Asn Leu Arg Glu Asn Gln Asn Asn Gln			
195	200	205	
Val Lys Lys Asp Lys Lys Ala Ala Lys Thr Leu Gly Ile Val Ile Gly			
210	215	220	
Val Phe Leu Leu Cys Trp Phe Pro Cys Phe Phe Thr Ile Leu Leu Asp			
225	230	235	240
Pro Phe Leu Asn Phe Ser Thr Pro Val Val Leu Phe Asp Ala Leu Thr			
245	250	255	
Trp Phe Gly Tyr Phe Asn Ser Thr Cys Asn Pro Leu Ile Tyr Gly Phe			
260	265	270	
Phe Tyr Pro Trp Phe Arg Arg Ala Leu Lys Tyr Ile Leu Leu Gly Lys			
275	280	285	
Ile Phe Ser Ser Cys Phe His Asn Thr Ile Leu Cys Met Gln Lys Glu			
290	295	300	
Ser Glu Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile			
305	310	315	320
Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser			
325	330	335	
Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe			
340	345	350	
Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr			
355	360	365	
Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met			
370	375	380	
Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln			

32/518

385                      390                      395                      400  
 Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala  
                          405                      410                      415  
 Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys  
                          420                      425                      430  
 Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu  
                          435                      440                      445  
 Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys  
                          450                      455                      460  
 Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly  
 465                      470                      475                      480  
 Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp  
                          485                      490                      495  
 Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala  
                          500                      505                      510  
 Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu  
                          515                      520                      525  
 Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
                          530                      535                      540

&lt;210&gt; 31

&lt;211&gt; 612

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 31

Met Pro Thr Leu Asn Thr Ser Ala Ser Pro Pro Thr Phe Phe Trp Ala  
                          5                      10                      15  
 Asn Ala Ser Gly Gly Ser Val Leu Ser Ala Asp Asp Ala Pro Met Pro

33/518

20	25	30
Val Lys Phe Leu Ala Leu Arg Leu Met Val Ala Leu Ala Tyr Gly Leu		
35	40	45
Val Gly Ala Ile Gly Leu Leu Gly Asn Leu Ala Val Leu Trp Val Leu		
50	55	60
Ser Asn Cys Ala Arg Arg Ala Pro Gly Pro Pro Ser Asp Thr Phe Val		
65	70	75
Phe Asn Leu Ala Leu Ala Asp Leu Gly Leu Ala Leu Thr Leu Pro Phe		
85	90	95
Trp Ala Ala Glu Ser Ala Leu Asp Phe His Trp Pro Phe Gly Gly Ala		
100	105	110
Leu Cys Lys Met Val Leu Thr Ala Thr Val Leu Asn Val Tyr Ala Ser		
115	120	125
Ile Phe Leu Ile Thr Ala Leu Ser Val Ala Arg Tyr Trp Val Val Ala		
130	135	140
Met Ala Ala Gly Pro Gly Thr His Leu Ser Leu Phe Trp Ala Arg Ile		
145	150	155
Ala Thr Leu Ala Val Trp Ala Ala Ala Ala Leu Val Thr Val Pro Thr		
165	170	175
Ala Val Phe Gly Val Glu Gly Glu Val Cys Gly Val Arg Leu Cys Leu		
180	185	190
Leu Arg Phe Pro Ser Arg Tyr Trp Leu Gly Ala Tyr Gln Leu Gln Arg		
195	200	205
Val Val Leu Ala Phe Met Val Pro Leu Gly Val Ile Thr Thr Ser Tyr		
210	215	220
Leu Leu Leu Leu Ala Phe Leu Gln Arg Arg Gln Arg Arg Arg Gln Asp		
225	230	235
Ser Arg Val Val Ala Arg Ser Val Arg Ile Leu Val Ala Ser Phe Phe		
245	250	255

34/518

Leu Cys Trp Phe Pro Asn His Val Val Thr Leu Trp Gly Val Leu Val  
 260 265 270  
 Lys Phe Asp Leu Val Pro Trp Asn Ser Thr Phe Tyr Thr Ile Gln Thr  
 275 280 285  
 Tyr Val Phe Pro Val Thr Thr Cys Leu Ala His Ser Asn Ser Cys Leu  
 290 295 300  
 Asn Pro Val Leu Tyr Cys Leu Leu Arg Arg Glu Pro Arg Gln Ala Leu  
 305 310 315 320  
 Ala Gly Thr Phe Arg Asp Leu Arg Ser Arg Leu Trp Pro Gln Gly Gly  
 325 330 335  
 Gly Trp Val Gln Gln Val Ala Leu Lys Gln Val Gly Arg Arg Trp Val  
 340 345 350  
 Ala Ser Asn Pro Arg Glu Ser Arg Pro Ser Thr Leu Leu Thr Asn Leu  
 355 360 365  
 Asp Arg Gly Thr Pro Gly Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly  
 370 375 380  
 Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys  
 385 390 395 400  
 Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu  
 405 410 415  
 Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro  
 420 425 430  
 Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr  
 435 440 445  
 Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu  
 450 455 460  
 Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr  
 465 470 475 480  
 Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg

35/518

	485	490	495
Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly			
500	505	510	
His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala			
515	520	525	
Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn			
530	535	540	
Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr			
545	550	555	560
Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser			
565	570	575	
Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met			
580	585	590	
Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp			
595	600	605	
Glu Leu Tyr Asn			
610			

&lt;210&gt; 32

&lt;211&gt; 599

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 32

Met Ser Pro Glu Cys Ala Arg Ala Ala Gly Asp Ala Pro Leu Arg Ser			
5	10	15	
Leu Glu Gln Ala Asn Arg Thr Arg Phe Pro Phe Phe Ser Asp Val Lys			
20	25	30	
Gly Asp His Arg Leu Val Leu Ala Ala Val Glu Thr Thr Val Leu Val			



36/518

35	40	45
Leu Ile Phe Ala Val Ser Leu Leu Gly Asn Val Cys Ala Leu Val Leu		
50	55	60
Val Ala Arg Arg Arg Arg Arg Gly Ala Thr Ala Cys Leu Val Leu Asn		
65	70	75
Leu Phe Cys Ala Asp Leu Leu Phe Ile Ser Ala Ile Pro Leu Val Leu		
85	90	95
Ala Val Arg Trp Thr Glu Ala Trp Leu Leu Gly Pro Val Ala Cys His		
100	105	110
Leu Leu Phe Tyr Val Met Thr Leu Ser Gly Ser Val Thr Ile Leu Thr		
115	120	125
Leu Ala Ala Val Ser Leu Glu Arg Met Val Cys Ile Val His Leu Gln		
130	135	140
Arg Gly Val Arg Gly Pro Gly Arg Arg Ala Arg Ala Val Leu Leu Ala		
145	150	155
Leu Ile Trp Gly Tyr Ser Ala Val Ala Ala Leu Pro Leu Cys Val Phe		
165	170	175
Phe Arg Val Val Pro Gln Arg Leu Pro Gly Ala Asp Gln Glu Ile Ser		
180	185	190
Ile Cys Thr Leu Ile Trp Pro Thr Ile Pro Gly Glu Ile Ser Trp Asp		
195	200	205
Val Ser Phe Val Thr Leu Asn Phe Leu Val Pro Gly Leu Val Ile Val		
210	215	220
Ile Ser Tyr Ser Lys Ile Leu Gln Ile Thr Lys Ala Ser Arg Lys Arg		
225	230	235
Leu Thr Val Ser Leu Ala Tyr Ser Glu Ser His Gln Ile Arg Val Ser		
245	250	255
Gln Gln Asp Phe Arg Leu Phe Arg Thr Leu Phe Leu Leu Met Val Ser		
260	265	270

37/518

Phe Phe Ile Met Trp Ser Pro Ile Ile Ile Thr Ile Leu Leu Ile Leu  
 275 280 285  
 Ile Gln Asn Phe Lys Gln Asp Leu Val Ile Trp Pro Ser Leu Phe Phe  
 290 295 300  
 Trp Val Val Ala Phe Thr Phe Ala Asn Ser Ala Leu Asn Pro Ile Leu  
 305 310 315 320  
 Tyr Asn Met Thr Leu Cys Arg Asn Glu Trp Lys Lys Ile Phe Cys Cys  
 325 330 335  
 Phe Trp Phe Pro Glu Lys Gly Ala Ile Leu Thr Asp Thr Ser Val Lys  
 340 345 350  
 Arg Asn Asp Leu Ser Ile Ile Ser Gly Ala Ser Lys Gly Glu Glu Leu  
 355 360 365  
 Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn  
 370 375 380  
 Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr  
 385 390 395 400  
 Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val  
 405 410 415  
 Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe  
 420 425 430  
 Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala  
 435 440 445  
 Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp  
 450 455 460  
 Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu  
 465 470 475 480  
 Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn  
 485 490 495  
 Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr

38/518

500                      505                      510  
 Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr  
 515                      520                      525  
 Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln  
 530                      535                      540  
 Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His  
 545                      550                      555                      560  
 Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg  
 565                      570                      575  
 Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His  
 580                      585                      590  
 Gly Met Asp Glu Leu Tyr Asn  
 595

&lt;210&gt; 33

&lt;211&gt; 890

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 33

Met Gln Gly Pro Leu Leu Leu Pro Gly Leu Cys Phe Leu Leu Ser Leu  
                     5                      10                      15  
 Phe Gly Ala Val Thr Gln Lys Thr Lys Thr Ser Cys Ala Lys Cys Pro  
                     20                      25                      30  
 Pro Asn Ala Ser Cys Val Asn Asn Thr His Cys Thr Cys Asn His Gly  
                     35                      40                      45  
 Tyr Thr Ser Gly Ser Gly Gln Lys Leu Phe Thr Phe Pro Leu Glu Thr  
                     50                      55                      60  
 Cys Asn Asp Ile Asn Glu Cys Thr Pro Pro Tyr Ser Val Tyr Cys Gly

39/518

65	70	75	80
Phe Asn Ala Val Cys Tyr Asn Val Glu Gly Ser Phe Tyr Cys Gln Cys			
85	90	95	
Val Pro Gly Tyr Arg Leu His Ser Gly Asn Glu Gln Phe Ser Asn Ser			
100	105	110	
Asn Glu Asn Thr Cys Gln Asp Thr Thr Ser Ser Lys Thr Thr Gln Gly			
115	120	125	
Arg Lys Glu Leu Gln Lys Ile Val Asp Lys Phe Glu Ser Leu Leu Thr			
130	135	140	
Asn Gln Thr Leu Trp Arg Thr Glu Gly Arg Gln Glu Ile Ser Ser Thr			
145	150	155	160
Ala Thr Thr Ile Leu Arg Asp Val Glu Ser Lys Val Leu Glu Thr Ala			
165	170	175	
Leu Lys Asp Pro Glu Gln Lys Val Leu Lys Ile Gln Asn Asp Ser Val			
180	185	190	
Ala Ile Glu Thr Gln Ala Ile Thr Asp Asn Cys Ser Glu Glu Arg Lys			
195	200	205	
Thr Phe Asn Leu Asn Val Gln Met Asn Ser Met Asp Ile Arg Cys Ser			
210	215	220	
Asp Ile Ile Gln Gly Asp Thr Gln Gly Pro Ser Ala Ile Ala Phe Ile			
225	230	235	240
Ser Tyr Ser Ser Leu Gly Asn Ile Ile Asn Ala Thr Phe Phe Glu Glu			
245	250	255	
Met Asp Lys Lys Asp Gln Val Tyr Leu Asn Ser Gln Val Val Ser Ala			
260	265	270	
Ala Ile Gly Pro Lys Arg Asn Val Ser Leu Ser Lys Ser Val Thr Leu			
275	280	285	
Thr Phe Gln His Val Lys Met Thr Pro Ser Thr Lys Lys Val Phe Cys			
290	295	300	

40/518

Val Tyr Trp Lys Ser Thr Gly Gln Gly Ser Gln Trp Ser Arg Asp Gly  
 305 310 315 320  
 Cys Phe Leu Ile His Val Asn Lys Ser His Thr Met Cys Asn Cys Ser  
 325 330 335  
 His Leu Ser Ser Phe Ala Val Leu Met Ala Leu Thr Ser Gln Glu Glu  
 340 345 350  
 Asp Pro Val Leu Thr Val Ile Thr Tyr Val Gly Leu Ser Val Ser Leu  
 355 360 365  
 Leu Cys Leu Leu Leu Ala Ala Leu Thr Phe Leu Leu Cys Lys Ala Ile  
 370 375 380  
 Gln Asn Thr Ser Thr Ser Leu His Leu Gln Leu Ser Leu Cys Leu Phe  
 385 390 395 400  
 Leu Ala His Leu Leu Phe Leu Val Gly Ile Asp Arg Thr Glu Pro Lys  
 405 410 415  
 Val Leu Cys Ser Ile Ile Ala Gly Ala Leu His Tyr Leu Tyr Leu Ala  
 420 425 430  
 Ala Phe Thr Trp Met Leu Leu Glu Gly Val His Leu Phe Leu Thr Ala  
 435 440 445  
 Arg Asn Leu Thr Val Val Asn Tyr Ser Ser Ile Asn Arg Leu Met Lys  
 450 455 460  
 Trp Ile Met Phe Pro Val Gly Tyr Gly Val Pro Ala Val Thr Val Ala  
 465 470 475 480  
 Ile Ser Ala Ala Ser Trp Pro His Leu Tyr Gly Thr Ala Asp Arg Cys  
 485 490 495  
 Trp Leu His Leu Asp Gln Gly Phe Met Trp Ser Phe Leu Gly Pro Val  
 500 505 510  
 Cys Ala Ile Phe Ser Ala Asn Leu Val Leu Phe Ile Leu Val Phe Trp  
 515 520 525  
 Ile Leu Lys Arg Lys Leu Ser Ser Leu Asn Ser Glu Val Ser Thr Ile

41/518

530	535	540
Gln Asn Thr Arg Met Leu Ala Phe Lys Ala Thr Ala Gln Leu Phe Ile		
545	550	555
Leu Gly Cys Thr Trp Cys Leu Gly Leu Leu Gln Val Gly Pro Ala Ala		560
565	570	575
Gln Val Met Ala Tyr Leu Phe Thr Ile Ile Asn Ser Leu Gln Gly Phe		
580	585	590
Phe Ile Phe Leu Val Tyr Cys Leu Leu Ser Gln Gln Val Gln Lys Gln		
595	600	605
Tyr Gln Lys Trp Phe Arg Glu Ile Val Lys Ser Lys Ser Glu Ser Glu		
610	615	620
Thr Tyr Thr Leu Ser Ser Lys Met Gly Pro Asp Ser Lys Pro Ser Glu		
625	630	635
Gly Asp Val Phe Pro Gly Gln Val Lys Arg Lys Tyr Ala Ser Lys Gly		640
645	650	655
Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly		
660	665	670
Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp		
675	680	685
Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys		
690	695	700
Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val		
705	710	715
Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe		720
725	730	735
Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe		
740	745	750
Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly		
755	760	765

42/518

Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu  
 770 775 780  
 Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His  
 785 790 795 800  
 Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn  
 805 810 815  
 Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp  
 820 825 830  
 His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro  
 835 840 845  
 Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn  
 850 855 860  
 Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly  
 865 870 875 880  
 Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
 885 890

&lt;210&gt; 34

&lt;211&gt; 598

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 34

Met Asp Pro Glu Glu Thr Ser Val Tyr Leu Asp Tyr Tyr Tyr Ala Thr  
 5 10 15  
 Ser Pro Asn Ser Asp Ile Arg Glu Thr His Ser His Val Pro Tyr Thr  
 20 25 30  
 Ser Val Phe Leu Pro Val Phe Tyr Thr Ala Val Phe Leu Thr Gly Val  
 35 40 45

43/518

Leu Gly Asn Leu Val Leu Met Gly Ala Leu His Phe Lys Pro Gly Ser  
 50 55 60  
 Arg Arg Leu Ile Asp Ile Phe Ile Ile Asn Leu Ala Ala Ser Asp Phe  
 65 70 75 80  
 Ile Phe Leu Val Thr Leu Pro Leu Trp Val Asp Lys Glu Ala Ser Leu  
 85 90 95  
 Gly Leu Trp Arg Thr Gly Ser Phe Leu Cys Lys Gly Ser Ser Tyr Met  
 100 105 110  
 Ile Ser Val Asn Met His Cys Ser Val Leu Leu Leu Thr Cys Met Ser  
 115 120 125  
 Val Asp Arg Tyr Leu Ala Ile Val Trp Pro Val Val Ser Arg Lys Phe  
 130 135 140  
 Arg Arg Thr Asp Cys Ala Tyr Val Val Cys Ala Ser Ile Trp Phe Ile  
 145 150 155 160  
 Ser Cys Leu Leu Gly Leu Pro Thr Leu Leu Ser Arg Glu Leu Thr Leu  
 165 170 175  
 Ile Asp Asp Lys Pro Tyr Cys Ala Glu Lys Lys Ala Thr Pro Ile Lys  
 180 185 190  
 Leu Ile Trp Ser Leu Val Ala Leu Ile Phe Thr Phe Phe Val Pro Leu  
 195 200 205  
 Leu Ser Ile Val Thr Cys Tyr Cys Cys Ile Ala Arg Lys Leu Cys Ala  
 210 215 220  
 His Tyr Gln Gln Ser Gly Lys His Asn Lys Lys Leu Lys Lys Ser Ile  
 225 230 235 240  
 Lys Ile Ile Phe Ile Val Val Ala Ala Phe Leu Val Ser Trp Leu Pro  
 245 250 255  
 Phe Asn Thr Phe Lys Phe Leu Ala Ile Val Ser Gly Leu Arg Gln Glu  
 260 265 270  
 His Tyr Leu Pro Ser Ala Ile Leu Gln Leu Gly Met Glu Val Ser Gly



44/518

275	280	285
Pro Leu Ala Phe Ala Asn Ser Cys Val Asn Pro Phe Ile Tyr Tyr Ile		
290	295	300
Phe Asp Ser Tyr Ile Arg Arg Ala Ile Val His Cys Leu Cys Pro Cys		
305	310	315
Leu Lys Asn Tyr Asp Phe Gly Ser Ser Thr Glu Thr Ser Asp Ser His		
325	330	335
Leu Thr Lys Ala Leu Ser Thr Phe Ile His Ala Glu Asp Phe Ala Arg		
340	345	350
Arg Arg Lys Arg Ser Val Ser Leu Ala Ser Lys Gly Glu Glu Leu Phe		
355	360	365
Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly		
370	375	380
His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly		
385	390	395
Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro		
405	410	415
Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser		
420	425	430
Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met		
435	440	445
Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly		
450	455	460
Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val		
465	470	475
Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile		
485	490	495
Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile		
500	505	510

45/518

Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg  
           515                  520                  525  
 His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln  
           530                  535                  540  
 Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr  
 545                  550                  555                  560  
 Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp  
                   565                  570                  575  
 His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly  
                   580                  585                  590  
 Met Asp Glu Leu Tyr Asn  
           595

&lt;210&gt; 35

&lt;211&gt; 557

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 35

Met Pro Phe Pro Asn Cys Ser Ala Pro Ser Thr Val Val Ala Thr Ala  
                   5                  10                  15  
 Val Gly Val Leu Leu Gly Leu Glu Cys Gly Leu Gly Leu Leu Gly Asn  
                   20                  25                  30  
 Ala Val Ala Leu Trp Thr Phe Leu Phe Arg Val Arg Val Trp Lys Pro  
                   35                  40                  45  
 Tyr Ala Val Tyr Leu Leu Asn Leu Ala Leu Ala Asp Leu Leu Leu Ala  
                   50                  55                  60  
 Ala Cys Leu Pro Phe Leu Ala Ala Phe Tyr Leu Ser Leu Gln Ala Trp  
                   65                  70                  75                  80

46/518

His Leu Gly Arg Val Gly Cys Trp Ala Leu Arg Phe Leu Leu Asp Leu  
                     85                    90                    95  
 Ser Arg Ser Val Gly Met Ala Phe Leu Ala Ala Val Ala Leu Asp Arg  
                     100                    105                    110  
 Tyr Leu Arg Val Val His Pro Arg Leu Lys Val Asn Leu Leu Ser Pro  
                     115                    120                    125  
 Gln Ala Ala Leu Gly Val Ser Gly Leu Val Trp Leu Leu Met Val Ala  
                     130                    135                    140  
 Leu Thr Cys Pro Gly Leu Leu Ile Ser Glu Ala Ala Gln Asn Ser Thr  
                     145                    150                    155                    160  
 Arg Cys His Ser Phe Tyr Ser Arg Ala Asp Gly Ser Phe Ser Ile Ile  
                     165                    170                    175  
 Trp Gln Glu Ala Leu Ser Cys Leu Gln Phe Val Leu Pro Phe Gly Leu  
                     180                    185                    190  
 Ile Val Phe Cys Asn Ala Gly Ile Ile Arg Ala Leu Gln Lys Arg Leu  
                     195                    200                    205  
 Arg Glu Pro Glu Lys Gln Pro Lys Leu Gln Arg Ala Gln Ala Leu Val  
                     210                    215                    220  
 Thr Leu Val Val Val Leu Phe Ala Leu Cys Phe Leu Pro Cys Phe Leu  
                     225                    230                    235                    240  
 Ala Arg Val Leu Met His Ile Phe Gln Asn Leu Gly Ser Cys Arg Ala  
                     245                    250                    255  
 Leu Cys Ala Val Ala His Thr Ser Asp Val Thr Gly Ser Leu Thr Tyr  
                     260                    265                    270  
 Leu His Ser Val Leu Asn Pro Val Val Tyr Cys Phe Ser Ser Pro Thr  
                     275                    280                    285  
 Phe Arg Ser Ser Tyr Arg Arg Val Phe His Thr Leu Arg Gly Lys Gly  
                     290                    295                    300  
 Gln Ala Ala Glu Pro Pro Asp Phe Asn Pro Arg Asp Ser Tyr Ser Ala

47/518

305	310	315	320
Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu			
	325	330	335
Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly			
	340	345	350
Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr			
	355	360	365
Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys			
	370	375	380
Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His			
385	390	395	400
Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr			
	405	410	415
Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys			
	420	425	430
Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp			
	435	440	445
Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr			
	450	455	460
Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile			
465	470	475	480
Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln			
	485	490	495
Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val			
	500	505	510
Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys			
	515	520	525
Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr			
	530	535	540

48/518

Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn

545

550

555

&lt;210&gt; 36

&lt;211&gt; 641

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 36

Met Phe Val Ala Ser Glu Arg Lys Met Arg Ala His Gln Val Leu Thr

5

10

15

Phe Leu Leu Leu Phe Val Ile Thr Ser Val Ala Ser Glu Asn Ala Ser

20

25

30

Thr Ser Arg Gly Cys Gly Leu Asp Leu Leu Pro Gln Tyr Val Ser Leu

35

40

45

Cys Asp Leu Asp Ala Ile Trp Gly Ile Val Val Glu Ala Val Ala Gly

50

55

60

Ala Gly Ala Leu Ile Thr Leu Leu Leu Met Leu Ile Leu Leu Val Arg

65

70

75

80

Leu Pro Phe Ile Lys Glu Lys Glu Lys Lys Ser Pro Val Gly Leu His

85

90

95

Phe Leu Phe Leu Leu Gly Thr Leu Gly Leu Phe Gly Leu Thr Phe Ala

100

105

110

Phe Ile Ile Gln Glu Asp Glu Thr Ile Cys Ser Val Arg Arg Phe Leu

115

120

125

Trp Gly Val Leu Phe Ala Leu Cys Phe Ser Cys Leu Leu Ser Gln Ala

130

135

140

Trp Arg Val Arg Arg Leu Val Arg His Gly Thr Gly Pro Ala Gly Trp

145

150

155

160

49/518

Gln Leu Val Gly Leu Ala Leu Cys Leu Met Leu Val Gln Val Ile Ile  
 165 170 175  
 Ala Val Glu Trp Leu Val Leu Thr Val Leu Arg Asp Thr Arg Pro Ala  
 180 185 190  
 Cys Ala Tyr Glu Pro Met Asp Phe Val Met Ala Leu Ile Tyr Asp Met  
 195 200 205  
 Val Leu Leu Val Val Thr Leu Gly Leu Ala Leu Phe Thr Leu Cys Gly  
 210 215 220  
 Lys Phe Lys Arg Trp Lys Leu Asn Gly Ala Phe Leu Leu Ile Thr Ala  
 225 230 235 240  
 Phe Leu Ser Val Leu Ile Trp Val Ala Trp Met Thr Met Tyr Leu Phe  
 245 250 255  
 Gly Asn Val Lys Leu Gln Gln Gly Asp Ala Trp Asn Asp Pro Thr Leu  
 260 265 270  
 Ala Ile Thr Leu Ala Ala Ser Gly Trp Val Phe Val Ile Phe His Ala  
 275 280 285  
 Ile Pro Glu Ile His Cys Thr Leu Leu Pro Ala Leu Gln Glu Asn Thr  
 290 295 300  
 Pro Asn Tyr Phe Asp Thr Ser Gln Pro Arg Met Arg Glu Thr Ala Phe  
 305 310 315 320  
 Glu Glu Asp Val Gln Leu Pro Arg Ala Tyr Met Glu Asn Lys Ala Phe  
 325 330 335  
 Ser Met Asp Glu His Asn Ala Ala Leu Arg Thr Ala Gly Phe Pro Asn  
 340 345 350  
 Gly Ser Leu Gly Lys Arg Pro Ser Gly Ser Leu Gly Lys Arg Pro Ser  
 355 360 365  
 Ala Pro Phe Arg Ser Asn Val Tyr Gln Pro Thr Glu Met Ala Val Val  
 370 375 380  
 Leu Asn Gly Gly Thr Ile Pro Thr Ala Pro Pro Ser His Thr Gly Arg

50/518

385	390	395	400
His Leu Trp Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro			
	405	410	415
Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val			
	420	425	430
Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys			
	435	440	445
Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val			
	450	455	460
Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His			
465	470	475	480
Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val			
	485	490	495
Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg			
	500	505	510
Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu			
	515	520	525
Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu			
	530	535	540
Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln			
545	550	555	560
Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp			
	565	570	575
Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly			
	580	585	590
Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser			
	595	600	605
Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu			
	610	615	620

51/518

Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr  
625 630 635 640  
Asn

&lt;210&gt; 37

&lt;211&gt; 581

&lt;212&gt; PRT

<213> Human

&lt;400&gt; 37

Met	Ala	Gly	Asn	Cys	Ser	Trp	Glu	Ala	His	Pro	Gly	Asn	Arg	Asn	Arg	
				5					10					15		
Met	Cys	Pro	Gly	Leu	Ser	Glu	Ala	Pro	Glu	Leu	Tyr	Ser	Arg	Gly	Phe	
				20					25					30		
Leu	Thr	Ile	Glu	Gln	Ile	Ala	Met	Leu	Pro	Pro	Pro	Ala	Val	Met	Asn	
				35					40					45		
Tyr	Ile	Phe	Leu	Leu	Leu	Cys	Leu	Cys	Gly	Leu	Val	Gly	Asn	Gly	Leu	
				50					55					60		
Val	Leu	Trp	Phe	Phe	Gly	Phe	Ser	Ile	Lys	Arg	Asn	Pro	Phe	Ser	Ile	
				65					70					75		
Tyr	Phe	Leu	His	Leu	Ala	Ser	Ala	Asp	Val	Gly	Tyr	Leu	Phe	Ser	Lys	
				85					90					95		
Ala	Val	Phe	Ser	Ile	Leu	Asn	Thr	Gly	Gly	Phe	Leu	Gly	Thr	Phe	Ala	
				100					105					110		
Asp	Tyr	Ile	Arg	Ser	Val	Cys	Arg	Val	Leu	Gly	Leu	Cys	Met	Phe	Leu	
				115					120					125		
Thr	Gly	Val	Ser	Leu	Leu	Pro	Ala	Val	Ser	Ala	Glu	Arg	Cys	Ala	Ser	
				130					135					140		
Val	Ile	Phe	Pro	Ala	Trp	Tyr	Trp	Arg	Arg	Arg	Pro	Lys	Arg	Leu	Ser	



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145	150	155	160
Ala Val Val Cys	Ala Leu Leu Trp Val Leu Ser Leu Leu Val Thr Cys		
165	170	175	
Leu His Asn Tyr Phe Cys Val Phe Leu Gly Arg Gly Ala Pro Gly Ala			
180	185	190	
Ala Cys Arg His Met Asp Ile Phe Leu Gly Ile Leu Leu Phe Leu Leu			
195	200	205	
Cys Cys Pro Leu Met Val Leu Pro Cys Leu Ala Leu Ile Leu His Val			
210	215	220	
Glu Cys Arg Ala Arg Arg Arg Gln Arg Ser Ala Lys Leu Asn His Val			
225	230	235	240
Ile Leu Ala Met Val Ser Val Phe Leu Val Ser Ser Ile Tyr Leu Gly			
245	250	255	
Ile Asp Trp Phe Leu Phe Trp Val Phe Gln Ile Pro Ala Pro Phe Pro			
260	265	270	
Glu Tyr Val Thr Asp Leu Cys Ile Cys Ile Asn Ser Ser Ala Lys Pro			
275	280	285	
Ile Val Tyr Phe Leu Ala Gly Arg Asp Lys Ser Gln Arg Leu Trp Glu			
290	295	300	
Pro Leu Arg Val Val Phe Gln Arg Ala Leu Arg Asp Gly Ala Glu Leu			
305	310	315	320
Gly Glu Ala Gly Gly Ser Thr Pro Asn Thr Val Thr Met Glu Met Gln			
325	330	335	
Cys Pro Pro Gly Asn Ala Ser Ala Ser Lys Gly Glu Glu Leu Phe Thr			
340	345	350	
Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His			
355	360	365	
Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys			
370	375	380	

53/518

Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp  
 385                      390                      395                      400  
 Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg  
                     405                      410                      415  
 Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro  
                     420                      425                      430  
 Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn  
                     435                      440                      445  
 Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn  
                     450                      455                      460  
 Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu  
 465                      470                      475                      480  
 Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met  
                     485                      490                      495  
 Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His  
                     500                      505                      510  
 Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn  
                     515                      520                      525  
 Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu  
                     530                      535                      540  
 Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His  
 545                      550                      555                      560  
 Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met  
                     565                      570                      575  
 Asp Glu Leu Tyr Asn  
                     580

&lt;210&gt; 38

&lt;211&gt; 1252

54/518

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 38

Met Val Phe Ser Val Arg Gln Cys Gly His Val Gly Arg Thr Glu Glu

5 10 15

Val Leu Leu Thr Phe Lys Ile Phe Leu Val Ile Ile Cys Leu His Val

20 25 30

Val Leu Val Thr Ser Leu Glu Glu Asp Thr Asp Asn Ser Ser Leu Ser

35 40 45

Pro Pro Pro Ala Lys Leu Ser Val Val Ser Phe Ala Pro Ser Ser Asn

50 55 60

Glu Val Glu Thr Thr Ser Leu Asn Asp Val Thr Leu Ser Leu Leu Pro

65 70 75 80

Ser Asn Glu Thr Glu Lys Thr Lys Ile Thr Ile Val Lys Thr Phe Asn

85 90 95

Ala Ser Gly Val Lys Pro Gln Arg Asn Ile Cys Asn Leu Ser Ser Ile

100 105 110

Cys Asn Asp Ser Ala Phe Phe Arg Gly Glu Ile Met Phe Gln Tyr Asp

115 120 125

Lys Glu Ser Thr Val Pro Gln Asn Gln His Ile Thr Asn Gly Thr Leu

130 135 140

Thr Gly Val Leu Ser Leu Ser Glu Leu Lys Arg Ser Glu Leu Asn Lys

145 150 155 160

Thr Leu Gln Thr Leu Ser Glu Thr Tyr Phe Ile Met Cys Ala Thr Ala

165 170 175

Glu Ala Gln Ser Thr Leu Asn Cys Thr Phe Thr Ile Lys Leu Asn Asn

180 185 190

Thr Met Asn Ala Cys Ala Val Ile Ala Ala Leu Glu Arg Val Lys Ile

55/518

195	200	205
Arg Pro Met Glu His Cys Cys Cys Ser Val Arg Ile Pro Cys Pro Ser		
210	215	220
Ser Pro Glu Glu Leu Glu Lys Leu Gln Cys Asp Leu Gln Asp Pro Ile		
225	230	235
Val Cys Leu Ala Asp His Pro Arg Gly Pro Pro Phe Ser Ser Ser Gln		
245	250	255
Ser Ile Pro Val Val Pro Arg Ala Thr Val Leu Ser Gln Val Pro Lys		
260	265	270
Ala Thr Ser Phe Ala Glu Pro Pro Asp Tyr Ser Pro Val Thr His Asn		
275	280	285
Val Pro Ser Pro Ile Gly Glu Ile Gln Pro Leu Ser Pro Gln Pro Ser		
290	295	300
Ala Pro Ile Ala Ser Ser Pro Ala Ile Asp Met Pro Pro Gln Ser Glu		
305	310	315
Thr Ile Ser Ser Pro Met Pro Gln Thr His Val Ser Gly Thr Pro Pro		
325	330	335
Pro Val Lys Ala Ser Phe Ser Ser Pro Thr Val Ser Ala Pro Ala Asn		
340	345	350
Val Asn Thr Thr Ser Ala Pro Pro Val Gln Thr Asp Ile Val Asn Thr		
355	360	365
Ser Ser Ile Ser Asp Leu Glu Asn Gln Val Leu Gln Met Glu Lys Ala		
370	375	380
Leu Ser Leu Gly Ser Leu Glu Pro Asn Leu Ala Gly Glu Met Ile Asn		
385	390	395
Gln Val Ser Arg Leu Leu His Ser Pro Pro Asp Met Leu Ala Pro Leu		
405	410	415
Ala Gln Arg Leu Leu Lys Val Val Asp Asp Ile Gly Leu Gln Leu Asn		
420	425	430

56/518

Phe Ser Asn Thr Thr Ile Ser Leu Thr Ser Pro Ser Leu Ala Leu Ala  
 435 440 445  
 Val Ile Arg Val Asn Ala Ser Ser Phe Asn Thr Thr Thr Phe Val Ala  
 450 455 460  
 Gln Asp Pro Ala Asn Leu Gln Val Ser Leu Glu Thr Gln Ala Pro Glu  
 465 470 475 480  
 Asn Ser Ile Gly Thr Ile Thr Leu Pro Ser Ser Leu Met Asn Asn Leu  
 485 490 495  
 Pro Ala His Asp Met Glu Leu Ala Ser Arg Val Gln Phe Asn Phe Phe  
 500 505 510  
 Glu Thr Pro Ala Leu Phe Gln Asp Pro Ser Leu Glu Asn Leu Ser Leu  
 515 520 525  
 Ile Ser Tyr Val Ile Ser Ser Ser Val Ala Asn Leu Thr Val Arg Asn  
 530 535 540  
 Leu Thr Arg Asn Val Thr Val Thr Leu Lys His Ile Asn Pro Ser Gln  
 545 550 555 560  
 Asp Glu Leu Thr Val Arg Cys Val Phe Trp Asp Leu Gly Arg Asn Gly  
 565 570 575  
 Gly Arg Gly Gly Trp Ser Asp Asn Gly Cys Ser Val Lys Asp Arg Arg  
 580 585 590  
 Leu Asn Glu Thr Ile Cys Thr Cys Ser His Leu Thr Ser Phe Gly Val  
 595 600 605  
 Leu Leu Asp Leu Ser Arg Thr Ser Val Leu Pro Ala Gln Met Met Ala  
 610 615 620  
 Leu Thr Phe Ile Thr Tyr Ile Gly Cys Gly Leu Ser Ser Ile Phe Leu  
 625 630 635 640  
 Ser Val Thr Leu Val Thr Tyr Ile Ala Phe Glu Lys Ile Arg Arg Asp  
 645 650 655  
 Tyr Pro Ser Lys Ile Leu Ile Gln Leu Cys Ala Ala Leu Leu Leu Leu

57/518

660	665	670	
Asn Leu Val Phe Leu Leu Asp Ser Trp Ile Ala Leu Tyr Lys Met Gln			
675	680	685	
Gly Leu Cys Ile Ser Val Ala Val Phe Leu His Tyr Phe Leu Leu Val			
690	695	700	
Ser Phe Thr Trp Met Gly Leu Glu Ala Phe His Met Tyr Leu Ala Leu			
705	710	715	720
Val Lys Val Phe Asn Thr Tyr Ile Arg Lys Tyr Ile Leu Lys Phe Cys			
725	730	735	
Ile Val Gly Trp Gly Val Pro Ala Val Val Val Thr Ile Ile Leu Thr			
740	745	750	
Ile Ser Pro Asp Asn Tyr Gly Leu Gly Ser Tyr Gly Lys Phe Pro Asn			
755	760	765	
Gly Ser Pro Asp Asp Phe Cys Trp Ile Asn Asn Asn Ala Val Phe Tyr			
770	775	780	
Ile Thr Val Val Gly Tyr Phe Cys Val Ile Phe Leu Leu Asn Val Ser			
785	790	795	800
Met Phe Ile Val Val Leu Val Gln Leu Cys Arg Ile Lys Lys Lys Lys			
805	810	815	
Gln Leu Gly Ala Gln Arg Lys Thr Ser Ile Gln Asp Leu Arg Ser Ile			
820	825	830	
Ala Gly Leu Thr Phe Leu Leu Gly Ile Thr Trp Gly Phe Ala Phe Phe			
835	840	845	
Ala Trp Gly Pro Val Asn Val Thr Phe Met Tyr Leu Phe Ala Ile Phe			
850	855	860	
Asn Thr Leu Gln Gly Phe Phe Ile Phe Ile Phe Tyr Cys Val Ala Lys			
865	870	875	880
Glu Asn Val Arg Lys Gln Trp Arg Arg Tyr Leu Cys Cys Gly Lys Leu			
885	890	895	

58/518

Arg Leu Ala Glu Asn Ser Asp Trp Ser Lys Thr Ala Thr Asn Gly Leu

900

905

910

Lys Lys Gln Thr Val Asn Gln Gly Val Ser Ser Ser Ser Asn Ser Leu

915

920

925

Gln Ser Ser Ser Asn Ser Thr Asn Ser Thr Thr Leu Leu Val Asn Asn

930

935

940

Asp Cys Ser Val His Ala Ser Gly Asn Gly Asn Ala Ser Thr Glu Arg

945

950

955

960

Asn Gly Val Ser Phe Ser Val Gln Asn Gly Asp Val Cys Leu His Asp

965

970

975

Phe Thr Gly Lys Gln His Met Phe Asn Glu Lys Glu Asp Ser Cys Asn

980

985

990

Gly Lys Gly Arg Met Ala Leu Arg Arg Thr Ser Lys Arg Gly Ser Leu

995

1000

1005

His Phe Ile Glu Gln Met Ser Ser Lys Gly Glu Glu Leu Phe Thr Gly

1010

1015

1020

Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys

1025

1030

1035

1040

Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu

1045

1050

1055

Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro

1060

1065

1070

Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr

1075

1080

1085

Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu

1090

1095

1100

Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr

1105

1110

1115

1120

Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg

59/518

1125	1130	1135	
Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly			
1140	1145	1150	
His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala			
1155	1160	1165	
Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn			
1170	1175	1180	
Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr			
1185	1190	1195	1200
Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser			
1205	1210	1215	
Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met			
1220	1225	1230	
Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp			
1235	1240	1245	
Glu Leu Tyr Asn			
1250			

&lt;210&gt; 39

&lt;211&gt; 655

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 39

Met Glu Ser Ser Pro Ile Pro Gln Ser Ser Gly Asn Ser Ser Thr Leu		
5	10	15
Gly Arg Val Pro Gln Thr Pro Gly Pro Ser Thr Ala Ser Gly Val Pro		
20	25	30
Glu Val Gly Leu Arg Asp Val Ala Ser Glu Ser Val Ala Leu Phe Phe		



60/518

35	40	45
Met Leu Leu Leu Asp Leu Thr Ala Val Ala Gly Asn Ala Ala Val Met		
50	55	60
Ala Val Ile Ala Lys Thr Pro Ala Leu Arg Lys Phe Val Phe Val Phe		
65	70	75
His Leu Cys Leu Val Asp Leu Leu Ala Ala Leu Thr Leu Met Pro Leu		
85	90	95
Ala Met Leu Ser Ser Ser Ala Leu Phe Asp His Ala Leu Phe Gly Glu		
100	105	110
Val Ala Cys Arg Leu Tyr Leu Phe Leu Ser Val Cys Phe Val Ser Leu		
115	120	125
Ala Ile Leu Ser Val Ser Ala Ile Asn Val Glu Arg Tyr Tyr Tyr Val		
130	135	140
Val His Pro Met Arg Tyr Glu Val Arg Met Thr Leu Gly Leu Val Ala		
145	150	155
Ser Val Leu Val Gly Val Trp Val Lys Ala Leu Ala Met Ala Ser Val		
165	170	175
Pro Val Leu Gly Arg Val Ser Trp Glu Glu Gly Ala Pro Ser Val Pro		
180	185	190
Pro Gly Cys Ser Leu Gln Trp Ser His Ser Ala Tyr Cys Gln Leu Phe		
195	200	205
Val Val Val Phe Ala Val Leu Tyr Phe Leu Leu Pro Leu Leu Leu Ile		
210	215	220
Leu Val Val Tyr Cys Ser Met Phe Arg Val Ala Arg Val Ala Ala Met		
225	230	235
Gln His Gly Pro Leu Pro Thr Trp Met Glu Thr Pro Arg Gln Arg Ser		
245	250	255
Glu Ser Leu Ser Ser Arg Ser Thr Met Val Thr Ser Ser Gly Ala Pro		
260	265	270

61/518

Gln Thr Thr Pro His Arg Thr Phe Gly Gly Gly Lys Ala Ala Val Val  
 275 280 285  
 Leu Leu Ala Val Gly Gly Gln Phe Leu Leu Cys Trp Leu Pro Tyr Phe  
 290 295 300  
 Ser Phe His Leu Tyr Val Ala Leu Ser Ala Gln Pro Ile Ser Thr Gly  
 305 310 315 320  
 Gln Val Glu Ser Val Val Thr Trp Ile Gly Tyr Phe Cys Phe Thr Ser  
 325 330 335  
 Asn Pro Phe Phe Tyr Gly Cys Leu Asn Arg Gln Ile Arg Gly Glu Leu  
 340 345 350  
 Ser Lys Gln Phe Val Cys Phe Phe Lys Pro Ala Pro Glu Glu Glu Leu  
 355 360 365  
 Arg Leu Pro Ser Arg Glu Gly Ser Ile Glu Glu Asn Phe Leu Gln Phe  
 370 375 380  
 Leu Gln Gly Thr Gly Cys Pro Ser Glu Ser Trp Val Ser Arg Pro Leu  
 385 390 395 400  
 Pro Ser Pro Lys Gln Glu Pro Pro Ala Val Asp Phe Arg Ile Gln Ala  
 405 410 415  
 Arg Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu  
 420 425 430  
 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly  
 435 440 445  
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile  
 450 455 460  
 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr  
 465 470 475 480  
 Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys  
 485 490 495  
 Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu

62/518

500	505	510	
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu			
515	520	525	
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly			
530	535	540	
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr			
545	550	555	560
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn			
565	570	575	
Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser			
580	585	590	
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly			
595	600	605	
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu			
610	615	620	
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe			
625	630	635	640
Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn			
645	650	655	

&lt;210&gt; 40

&lt;211&gt; 573

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 40

Met Gln Pro Ser Pro Pro Pro Thr Glu Leu Val Pro Ser Glu Arg Ala
5 10 15
Val Val Leu Leu Ser Cys Ala Leu Ser Ala Leu Gly Ser Gly Leu Leu

63/518

	20	25	30
Val	Ala	Thr	His
Ala	Leu	Trp	Pro
Asp	Leu	Arg	Ser
Arg	Ala	Arg	Arg
	35	40	45
Leu	Leu	Leu	Phe
Leu	Ser	Leu	Ala
Asp	Leu	Leu	Ser
Ala	Ala	Ser	Tyr
	50	55	60
Phe	Tyr	Gly	Val
Leu	Gln	Asn	Phe
Ala	Gly	Pro	Ser
Trp	Asp	Cys	Val
	65	70	75
Leu	Gln	Gly	Ala
Leu	Ser	Thr	Phe
Ala	Asn	Thr	Ser
Ser	Ser	Phe	Phe
Trp			
	85	90	95
Thr	Val	Ala	Ile
Ala	Leu	Tyr	Leu
Tyr	Leu	Ser	Ile
Val	Arg	Ala	Ala
	100	105	110
Arg	Gly	Pro	Arg
Thr	Asp	Arg	Leu
Leu	Trp	Ala	Phe
His	Val	Val	Ser
	115	120	125
Trp	Gly	Val	Pro
Leu	Val	Ile	Thr
Val	Ala	Ala	Val
Ala	Leu	Lys	Lys
	130	135	140
Ile	Gly	Tyr	Asp
Ala	Ser	Asp	Val
Ser	Val	Gly	Trp
Cys	Trp	Ile	Asp
	145	150	155
Leu	Glu	Ala	Lys
Asp	His	Val	Leu
Trp	Met	Leu	Leu
Thr	Gly	Lys	Leu
	165	170	175
Trp	Glu	Met	Leu
Ala	Tyr	Val	Leu
Leu	Pro	Leu	Leu
Tyr	Leu	Leu	Val
	180	185	190
Arg	Lys	His	Ile
Asn	Arg	Ala	His
Thr	Ala	Leu	Ser
Glu	Tyr	Arg	Pro
	195	200	205
Ile	Leu	Ser	Gln
Glu	His	Arg	Leu
Leu	Arg	His	Ser
Ser	Ser	Met	Ala
Asp			
	210	215	220
Lys	Lys	Leu	Val
Leu	Ile	Pro	Leu
Ile	Phe	Ile	Gly
Leu	Arg	Val	Trp
	225	230	235
Ser	Thr	Val	Arg
Phe	Val	Leu	Thr
Leu	Cys	Gly	Ser
Pro	Ala	Val	Gln
	245	250	255

64/518

Thr Pro Val Leu Val Val Leu His Gly Ile Gly Asn Thr Phe Gln Gly  
 260 265 270  
 Gly Ala Asn Cys Ile Met Phe Val Leu Cys Thr Arg Ala Val Arg Thr  
 275 280 285  
 Arg Leu Phe Ser Leu Cys Cys Cys Cys Cys Ser Ser Gln Pro Pro Thr  
 290 295 300  
 Lys Ser Pro Ala Gly Thr Pro Lys Ala Pro Ala Pro Ser Lys Pro Gly  
 305 310 315 320  
 Glu Ser Gln Glu Ser Gln Gly Thr Pro Gly Glu Leu Pro Ser Thr Ala  
 325 330 335  
 Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu  
 340 345 350  
 Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly  
 355 360 365  
 Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr  
 370 375 380  
 Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys  
 385 390 395 400  
 Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His  
 405 410 415  
 Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr  
 420 425 430  
 Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys  
 435 440 445  
 Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp  
 450 455 460  
 Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr  
 465 470 475 480  
 Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile

65/518

	485	490	495
Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln			
	500	505	510
Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val			
	515	520	525
Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys			
	530	535	540
Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr			
	545	550	555
Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn			560
	565	570	

&lt;210&gt; 41

&lt;211&gt; 920

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 41

Met Ala Val Arg Leu Cys Ser Leu Ser Leu Tyr Gly Glu Ile Glu Leu			
	5	10	15
Gln Lys Val Thr Ile Gly Asn Cys Asn Glu Asn Leu Glu Thr Leu Glu			
	20	25	30
Lys Gln Val Lys Asp Val Thr Ala Pro Leu Asn Asn Ile Ser Ser Glu			
	35	40	45
Val Gln Ile Leu Thr Ser Asp Ala Asn Lys Leu Thr Ala Glu Asn Ile			
	50	55	60
Thr Ser Ala Thr Arg Val Val Gly Gln Ile Phe Asn Thr Ser Arg Asn			
	65	70	75
Ala Ser Pro Glu Ala Lys Lys Val Ala Ile Val Thr Val Ser Gln Leu			80

66/518

	85	90	95
Leu Asp Ala Ser Glu Asp Ala Phe Gln Arg Val Ala Ala Thr Ala Asn			
100	105	110	
Asp Asp Ala Leu Thr Thr Leu Ile Glu Gln Met Glu Thr Tyr Ser Leu			
115	120	125	
Ser Leu Gly Asn Gln Ser Val Val Glu Pro Asn Ile Ala Ile Gln Ser			
130	135	140	
Ala Asn Phe Ser Ser Glu Asn Ala Val Gly Pro Ser Asn Val Arg Phe			
145	150	155	160
Ser Val Gln Lys Gly Ala Ser Ser Ser Leu Val Ser Ser Ser Thr Phe			
165	170	175	
Ile His Thr Asn Val Asp Gly Leu Asn Pro Asp Ala Gln Thr Glu Leu			
180	185	190	
Gln Val Leu Leu Asn Met Thr Lys Asn Tyr Thr Lys Thr Cys Gly Phe			
195	200	205	
Val Val Tyr Gln Asn Asp Lys Leu Phe Gln Ser Lys Thr Phe Thr Ala			
210	215	220	
Lys Ser Asp Phe Ser Gln Lys Ile Ile Ser Ser Lys Thr Asp Glu Asn			
225	230	235	240
Glu Gln Asp Gln Ser Ala Ser Val Asp Met Val Phe Ser Pro Lys Tyr			
245	250	255	
Asn Gln Lys Glu Phe Gln Leu Tyr Ser Tyr Ala Cys Val Tyr Trp Asn			
260	265	270	
Leu Ser Ala Lys Asp Trp Asp Thr Tyr Gly Cys Gln Lys Asp Lys Gly			
275	280	285	
Thr Asp Gly Phe Leu Arg Cys Arg Cys Asn His Thr Thr Asn Phe Ala			
290	295	300	
Val Leu Met Thr Phe Lys Lys Asp Tyr Gln Tyr Pro Lys Ser Leu Asp			
305	310	315	320

67/518

Ile Leu Ser Asn Val Gly Cys Ala Leu Ser Val Thr Gly Leu Ala Leu  
                   325                  330                  335  
 Thr Val Ile Phe Gln Ile Val Thr Arg Lys Val Arg Lys Thr Ser Val  
                   340                  345                  350  
 Thr Trp Val Leu Val Asn Leu Cys Ile Ser Met Leu Ile Phe Asn Leu  
                   355                  360                  365  
 Leu Phe Val Phe Gly Ile Glu Asn Ser Asn Lys Asn Leu Gln Thr Ser  
                   370                  375                  380  
 Asp Gly Asp Ile Asn Asn Ile Asp Phe Asp Asn Asn Asp Ile Pro Arg  
 385                  390                  395                  400  
 Thr Asp Thr Ile Asn Ile Pro Asn Pro Met Cys Thr Ala Ile Ala Ala  
                   405                  410                  415  
 Leu Leu His Tyr Phe Leu Leu Val Thr Phe Thr Trp Asn Ala Leu Ser  
                   420                  425                  430  
 Ala Ala Gln Leu Tyr Tyr Leu Leu Ile Arg Thr Met Lys Pro Leu Pro  
                   435                  440                  445  
 Arg His Phe Ile Leu Phe Ile Ser Leu Ile Gly Trp Gly Val Pro Ala  
                   450                  455                  460  
 Ile Val Val Ala Ile Thr Val Gly Val Ile Tyr Ser Gln Asn Gly Asn  
 465                  470                  475                  480  
 Asn Pro Gln Trp Glu Leu Asp Tyr Arg Gln Glu Lys Ile Cys Trp Leu  
                   485                  490                  495  
 Ala Ile Pro Glu Pro Asn Gly Val Ile Lys Ser Pro Leu Leu Trp Ser  
                   500                  505                  510  
 Phe Ile Val Pro Val Thr Ile Ile Leu Ile Ser Asn Val Val Met Phe  
                   515                  520                  525  
 Ile Thr Ile Ser Ile Lys Val Leu Trp Lys Asn Asn Gln Asn Leu Thr  
                   530                  535                  540  
 Ser Thr Lys Lys Val Ser Ser Met Lys Lys Ile Val Ser Thr Leu Ser



68/518

545	550	555	560
Val Ala Val Val Phe Gly Ile Thr Trp Ile Leu Ala Tyr Leu Met Leu			
	565	570	575
Val Asn Asp Asp Ser Ile Arg Ile Val Phe Ser Tyr Ile Phe Cys Leu			
	580	585	590
Phe Asn Thr Thr Gln Gly Leu Gln Ile Phe Ile Leu Tyr Thr Val Arg			
	595	600	605
Thr Lys Val Phe Gln Ser Glu Ala Ser Lys Val Leu Met Leu Leu Ser			
	610	615	620
Ser Ile Gly Arg Arg Lys Ser Leu Pro Ser Val Thr Arg Pro Arg Leu			
	625	630	635
Arg Val Lys Met Tyr Asn Phe Leu Arg Ser Leu Pro Thr Leu His Glu			
	645	650	655
Arg Phe Arg Leu Leu Glu Thr Ser Pro Ser Thr Glu Glu Ile Thr Leu			
	660	665	670
Ser Glu Ser Asp Asn Ala Lys Glu Ser Ile Ala Ser Lys Gly Glu Glu			
	675	680	685
Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val			
	690	695	700
Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr			
	705	710	715
Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro			
	725	730	735
Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys			
	740	745	750
Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser			
	755	760	765
Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp			
	770	775	780

69/518

Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr
785                      790                      795                      800
Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly
805                      810                      815
Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val
820                      825                      830
Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys
835                      840                      845
Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr
850                      855                      860
Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn
865                      870                      875                      880
His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys
885                      890                      895
Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr
900                      905                      910
His Gly Met Asp Glu Leu Tyr Asn
915                      920

&lt;210&gt; 42

<211> 766

&lt;212&gt; PRT

〈213〉 Human

<400> 42

Met Asp His Cys Gly Ala Leu Phe Leu Cys Leu Cys Leu Leu Thr Leu  
5 10 15  
Gln Asn Ala Thr Thr Glu Thr Trp Glu Glu Leu Leu Ser Tyr Met Glu  
20 25 30

70/518

Asn Met Gln Val Ser Arg Gly Arg Ser Ser Val Phe Ser Ser Arg Gln  
 35 40 45  
 Leu His Gln Leu Glu Gln Met Leu Leu Asn Thr Ser Phe Pro Gly Tyr  
 50 55 60  
 Asn Leu Thr Leu Gln Thr Pro Thr Ile Gln Ser Leu Ala Phe Lys Leu  
 65 70 75 80  
 Ser Cys Asp Phe Ser Gly Leu Ser Leu Thr Ser Ala Thr Leu Lys Arg  
 85 90 95  
 Val Pro Gln Ala Gly Gly Gln His Ala Arg Gly Gln His Ala Met Gln  
 100 105 110  
 Phe Pro Ala Glu Leu Thr Arg Asp Ala Cys Lys Thr Arg Pro Arg Glu  
 115 120 125  
 Leu Arg Leu Ile Cys Ile Tyr Phe Ser Asn Thr His Phe Phe Lys Asp  
 130 135 140  
 Glu Asn Asn Ser Ser Leu Leu Asn Asn Tyr Val Leu Gly Ala Gln Leu  
 145 150 155 160  
 Ser His Gly His Val Asn Asn Leu Arg Asp Pro Val Asn Ile Ser Phe  
 165 170 175  
 Trp His Asn Gln Ser Leu Glu Gly Tyr Thr Leu Thr Cys Val Phe Trp  
 180 185 190  
 Lys Glu Gly Ala Arg Lys Gln Pro Trp Gly Gly Trp Ser Pro Glu Gly  
 195 200 205  
 Cys Arg Thr Glu Gln Pro Ser His Ser Gln Val Leu Cys Arg Cys Asn  
 210 215 220  
 His Leu Thr Tyr Phe Ala Val Leu Met Gln Leu Ser Pro Ala Leu Val  
 225 230 235 240  
 Pro Ala Glu Leu Leu Ala Pro Leu Thr Tyr Ile Ser Leu Val Gly Cys  
 245 250 255  
 Ser Ile Ser Ile Val Ala Ser Leu Ile Thr Val Leu Leu His Phe His

71/518

260	265	270
Phe Arg Lys Gln Ser Asp Ser Leu Thr Arg Ile His Met Asn Leu His		
275	280	285
Ala Ser Val Leu Leu Leu Asn Ile Ala Phe Leu Leu Ser Pro Ala Phe		
290	295	300
Ala Met Ser Pro Val Pro Gly Ser Ala Cys Thr Ala Leu Ala Ala Ala		
305	310	315
Leu His Tyr Ala Leu Leu Ser Cys Leu Thr Trp Met Ala Ile Glu Gly		
325	330	335
Phe Asn Leu Tyr Leu Leu Leu Gly Arg Val Tyr Asn Ile Tyr Ile Arg		
340	345	350
Arg Tyr Val Phe Lys Leu Gly Val Leu Gly Trp Gly Ala Pro Ala Leu		
355	360	365
Leu Val Leu Leu Ser Leu Ser Val Lys Ser Ser Val Tyr Gly Pro Cys		
370	375	380
Thr Ile Pro Val Phe Asp Ser Trp Glu Asn Gly Thr Gly Phe Gln Asn		
385	390	395
Met Ser Ile Cys Trp Val Arg Ser Pro Val Val His Ser Val Leu Val		
405	410	415
Met Gly Tyr Gly Gly Leu Thr Ser Leu Phe Asn Leu Val Val Leu Ala		
420	425	430
Trp Ala Leu Trp Thr Leu Arg Arg Leu Arg Glu Arg Ala Asp Ala Pro		
435	440	445
Ser Val Arg Ala Cys His Asp Thr Val Thr Val Leu Gly Leu Thr Val		
450	455	460
Leu Leu Gly Thr Thr Trp Ala Leu Ala Phe Phe Ser Phe Gly Val Phe		
465	470	475
Leu Leu Pro Gln Leu Phe Leu Phe Thr Ile Leu Asn Ser Leu Tyr Gly		
485	490	495

72/518

Phe Phe Leu Phe Leu Trp Phe Cys Ser Gln Arg Cys Arg Ser Glu Ala  
                   500                  505                  510  
 Glu Ala Lys Ala Gln Ile Glu Ala Phe Ser Ser Ser Gln Thr Thr Gln  
                   515                  520                  525  
 Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val  
                   530                  535                  540  
 Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu  
 545                  550                  555                  560  
 Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys  
                   565                  570                  575  
 Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu  
                   580                  585                  590  
 Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg  
                   595                  600                  605  
 His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg  
                   610                  615                  620  
 Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val  
 625                  630                  635                  640  
 Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile  
                   645                  650                  655  
 Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn  
                   660                  665                  670  
 Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly  
                   675                  680                  685  
 Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val  
                   690                  695                  700  
 Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro  
 705                  710                  715                  720  
 Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser

73/518

	725		730		735										
Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe	Val
	740		745		750										
Thr	Ala	Ala	Gly	Ile	Thr	His	Gly	Met	Asp	Glu	Leu	Tyr	Asn		
	755		760		765										

&lt;210&gt; 43

&lt;211&gt; 1124

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 43

Met	Arg	Gly	Phe	Asn	Leu	Leu	Leu	Phe	Trp	Gly	Cys	Cys	Val	Met	His
				5					10					15	
Ser	Trp	Glu	Gly	His	Ile	Arg	Pro	Thr	Arg	Lys	Pro	Asn	Thr	Lys	Gly
			20					25					30		
Asn	Asn	Cys	Arg	Asp	Ser	Thr	Leu	Cys	Pro	Ala	Tyr	Ala	Thr	Cys	Thr
		35					40				45				
Asn	Thr	Val	Asp	Ser	Tyr	Tyr	Cys	Thr	Cys	Lys	Gln	Gly	Phe	Leu	Ser
	50					55				60					
Ser	Asn	Gly	Gln	Asn	His	Phe	Lys	Asp	Pro	Gly	Val	Arg	Cys	Lys	Asp
	65				70				75				80		
Ile	Asp	Glu	Cys	Ser	Gln	Ser	Pro	Gln	Pro	Cys	Gly	Pro	Asn	Ser	Ser
				85				90					95		
Cys	Lys	Asn	Leu	Ser	Gly	Arg	Tyr	Lys	Cys	Ser	Cys	Leu	Asp	Gly	Phe
		100						105					110		
Ser	Ser	Pro	Thr	Gly	Asn	Asp	Trp	Val	Pro	Gly	Lys	Pro	Gly	Asn	Phe
		115					120						125		
Ser	Cys	Thr	Asp	Ile	Asn	Glu	Cys	Leu	Thr	Ser	Arg	Val	Cys	Pro	Glu

74/518

130	135	140	
His Ser Asp Cys Val Asn Ser Met Gly Ser Tyr Ser Cys Ser Cys Gln			
145	150	155	160
Val Gly Phe Ile Ser Arg Asn Ser Thr Cys Glu Asp Val Asn Glu Cys			
	165	170	175
Ala Asp Pro Arg Ala Cys Pro Glu His Ala Thr Cys Asn Asn Thr Val			
	180	185	190
Gly Asn Tyr Ser Cys Phe Cys Asn Pro Gly Phe Glu Ser Ser Ser Gly			
	195	200	205
His Leu Ser Phe Gln Gly Leu Lys Ala Ser Cys Glu Asp Ile Asp Glu			
	210	215	220
Cys Thr Glu Met Cys Pro Ile Asn Ser Thr Cys Thr Asn Thr Pro Gly			
225	230	235	240
Ser Tyr Phe Cys Thr Cys His Pro Gly Phe Ala Pro Ser Ser Gly Gln			
	245	250	255
Leu Asn Phe Thr Asp Gln Gly Val Glu Cys Arg Asp Ile Asp Glu Cys			
	260	265	270
Arg Gln Asp Pro Ser Thr Cys Gly Pro Asn Ser Ile Cys Thr Asn Ala			
	275	280	285
Leu Gly Ser Tyr Ser Cys Gly Cys Ile Val Gly Phe His Pro Asn Pro			
	290	295	300
Glu Gly Ser Gln Lys Asp Gly Asn Phe Ser Cys Gln Arg Val Leu Phe			
305	310	315	320
Lys Cys Lys Glu Asp Val Ile Pro Asp Asn Lys Gln Ile Gln Gln Cys			
	325	330	335
Gln Glu Gly Thr Ala Val Lys Pro Ala Tyr Val Ser Phe Cys Ala Gln			
	340	345	350
Ile Asn Asn Ile Phe Ser Val Leu Asp Lys Val Cys Glu Asn Lys Thr			
	355	360	365

75/518

Thr Val Val Ser Leu Lys Asn Thr Thr Glu Ser Phe Val Pro Val Leu  
 370 375 380  
 Lys Gln Ile Ser Thr Trp Thr Lys Phe Thr Lys Glu Glu Thr Ser Ser  
 385 390 395 400  
 Leu Ala Thr Val Phe Leu Glu Ser Val Glu Ser Met Thr Leu Ala Ser  
 405 410 415  
 Phe Trp Lys Pro Ser Ala Asn Val Thr Pro Ala Val Arg Thr Glu Tyr  
 420 425 430  
 Leu Asp Ile Glu Ser Lys Val Ile Asn Lys Glu Cys Ser Glu Glu Asn  
 435 440 445  
 Val Thr Leu Asp Leu Val Ala Lys Gly Asp Lys Met Lys Ile Gly Cys  
 450 455 460  
 Ser Thr Ile Glu Glu Ser Glu Ser Thr Glu Thr Thr Gly Val Ala Phe  
 465 470 475 480  
 Val Ser Phe Val Gly Met Glu Ser Val Leu Asn Glu Arg Phe Phe Gln  
 485 490 495  
 Asp His Gln Ala Pro Leu Thr Thr Ser Glu Ile Lys Leu Lys Met Asn  
 500 505 510  
 Ser Arg Val Val Gly Gly Ile Met Thr Gly Glu Lys Lys Asp Gly Phe  
 515 520 525  
 Ser Asp Pro Ile Ile Tyr Thr Leu Glu Asn Val Gln Pro Lys Gln Lys  
 530 535 540  
 Phe Glu Arg Pro Ile Cys Val Ser Trp Ser Thr Asp Val Lys Gly Gly  
 545 550 555 560  
 Arg Trp Thr Ser Phe Gly Cys Val Ile Leu Glu Ala Ser Glu Thr Tyr  
 565 570 575  
 Thr Ile Cys Ser Cys Asn Gln Met Ala Asn Leu Ala Val Ile Met Ala  
 580 585 590  
 Ser Gly Glu Leu Thr Met Asp Phe Ser Leu Tyr Ile Ile Ser His Val



76/518

595	600	605
Gly Ile Ile Ile Ser Leu Val Cys Leu Val Leu Ala Ile Ala Thr Phe		
610	615	620
Leu Leu Cys Arg Ser Ile Arg Asn His Asn Thr Tyr Leu His Leu His		
625	630	635
Leu Cys Val Cys Leu Leu Leu Ala Lys Thr Leu Phe Leu Ala Gly Ile		
645	650	655
His Lys Thr Asp Asn Lys Thr Gly Cys Ala Ile Ile Ala Gly Phe Leu		
660	665	670
His Tyr Leu Phe Leu Ala Cys Phe Phe Trp Met Leu Val Glu Ala Val		
675	680	685
Ile Leu Phe Leu Met Val Arg Asn Leu Lys Val Val Asn Tyr Phe Ser		
690	695	700
Ser Arg Asn Ile Lys Met Leu His Ile Cys Ala Phe Gly Tyr Gly Leu		
705	710	715
Pro Met Leu Val Val Val Ile Ser Ala Ser Val Gln Pro Gln Gly Tyr		
725	730	735
Gly Met His Asn Arg Cys Trp Leu Asn Thr Glu Thr Gly Phe Ile Trp		
740	745	750
Ser Phe Leu Gly Pro Val Cys Thr Val Ile Val Ile Asn Ser Leu Leu		
755	760	765
Leu Thr Trp Thr Leu Trp Ile Leu Arg Gln Arg Leu Ser Ser Val Asn		
770	775	780
Ala Glu Val Ser Thr Leu Lys Asp Thr Arg Leu Leu Thr Phe Lys Ala		
785	790	795
Phe Ala Gln Leu Phe Ile Leu Gly Cys Ser Trp Val Leu Gly Ile Phe		
805	810	815
Gln Ile Gly Pro Val Ala Gly Val Met Ala Tyr Leu Phe Thr Ile Ile		
820	825	830

77/518

Asn Ser Leu Gln Gly Ala Phe Ile Phe Leu Ile His Cys Leu Leu Asn  
 835 840 845  
 Gly Gln Val Arg Glu Glu Tyr Lys Arg Trp Ile Thr Gly Lys Thr Lys  
 850 855 860  
 Pro Ser Ser Gln Ser Gln Thr Ser Arg Ile Leu Leu Ser Ser Met Pro  
 865 870 875 880  
 Ser Ala Ser Lys Thr Gly Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly  
 885 890 895  
 Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys  
 900 905 910  
 Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu  
 915 920 925  
 Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro  
 930 935 940  
 Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr  
 945 950 955 960  
 Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu  
 965 970 975  
 Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr  
 980 985 990  
 Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg  
 995 1000 1005  
 Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly  
 1010 1015 1020  
 His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala  
 1025 1030 1035 1040  
 Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn  
 1045 1050 1055  
 Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr

78/518

1060	1065	1070	
Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser			
1075	1080	1085	
Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met			
1090	1095	1100	
Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp			
1105	1110	1115	1120
Glu Leu Tyr Asn			

&lt;210&gt; 44

&lt;211&gt; 599

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 44

Met Ala Pro Thr Glu Pro Trp Ser Pro Ser Pro Gly Ser Ala Pro Trp
5 10 15
Asp Tyr Ser Gly Leu Asp Gly Leu Glu Glu Leu Glu Leu Cys Pro Ala
20 25 30
Gly Asp Leu Pro Tyr Gly Tyr Val Tyr Ile Pro Ala Leu Tyr Leu Ala
35 40 45
Ala Phe Ala Val Gly Leu Leu Gly Asn Ala Phe Val Val Trp Leu Leu
50 55 60
Ala Gly Arg Arg Gly Pro Arg Arg Leu Val Asp Thr Phe Val Leu His
65 70 75 80
Leu Ala Ala Ala Asp Leu Gly Phe Val Leu Thr Leu Pro Leu Trp Ala
85 90 95
Ala Ala Ala Ala Leu Gly Gly Arg Trp Pro Phe Gly Asp Gly Leu Cys
100 105 110

79/518

Lys Leu Ser Ser Phe Ala Leu Ala Gly Thr Arg Cys Ala Gly Ala Leu  
 115 120 125  
 Leu Leu Ala Gly Met Ser Val Asp Arg Tyr Leu Ala Val Val Lys Leu  
 130 135 140  
 Leu Glu Ala Arg Pro Leu Arg Thr Pro Arg Cys Ala Leu Ala Ser Cys  
 145 150 155 160  
 Cys Gly Val Trp Ala Val Ala Leu Leu Ala Gly Leu Pro Ser Leu Val  
 165 170 175  
 Tyr Arg Gly Leu Gln Pro Leu Pro Gly Gly Gln Asp Ser Gln Cys Gly  
 180 185 190  
 Glu Glu Pro Ser His Ala Phe Gln Gly Leu Ser Leu Leu Leu Leu Leu  
 195 200 205  
 Leu Thr Phe Val Leu Pro Leu Val Val Thr Leu Phe Cys Tyr Cys Arg  
 210 215 220  
 Ile Ser Arg Arg Leu Arg Arg Pro Pro His Val Gly Arg Ala Arg Arg  
 225 230 235 240  
 Asn Ser Leu Arg Ile Ile Phe Ala Ile Glu Ser Thr Phe Val Gly Ser  
 245 250 255  
 Trp Leu Pro Phe Ser Ala Leu Arg Ala Val Phe His Leu Ala Arg Leu  
 260 265 270  
 Gly Ala Leu Pro Leu Pro Cys Pro Leu Leu Leu Ala Leu Arg Trp Gly  
 275 280 285  
 Leu Thr Ile Ala Thr Cys Leu Ala Phe Val Asn Ser Cys Ala Asn Pro  
 290 295 300  
 Leu Ile Tyr Leu Leu Leu Asp Arg Ser Phe Arg Ala Arg Ala Leu Asp  
 305 310 315 320  
 Gly Ala Cys Gly Arg Thr Gly Arg Leu Ala Arg Arg Ile Ser Ser Ala  
 325 330 335  
 Ser Ser Leu Ser Arg Asp Asp Ser Ser Val Phe Arg Cys Arg Ala Gln

80/518

340	345	350	
Ala Ala Asn Thr Ala Ser Ala Ser Trp Ala Ser Lys Gly Glu Glu Leu			
355	360	365	
Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn			
370	375	380	
Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr			
385	390	395	400
Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val			
405	410	415	
Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe			
420	425	430	
Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala			
435	440	445	
Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp			
450	455	460	
Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu			
465	470	475	480
Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn			
485	490	495	
Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr			
500	505	510	
Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr			
515	520	525	
Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln			
530	535	540	
Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His			
545	550	555	560
Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg			
565	570	575	

81/518

Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His

580

585

590

Gly Met Asp Glu Leu Tyr Asn

595

&lt;210&gt; 45

&lt;211&gt; 557

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 45

Met Ser Gln Gln Asn Thr Ser Gly Asp Cys Leu Phe Asp Gly Val Asn

5

10

15

Glu Leu Met Lys Thr Leu Gln Phe Ala Val His Ile Pro Thr Phe Val

20

25

30

Leu Gly Leu Leu Leu Asn Leu Leu Ala Ile His Gly Phe Ser Thr Phe

35

40

45

Leu Lys Asn Arg Trp Pro Asp Tyr Ala Ala Thr Ser Ile Tyr Met Ile

50

55

60

Asn Leu Ala Val Phe Asp Leu Leu Leu Val Leu Ser Leu Pro Phe Lys

65

70

75

80

Met Val Leu Ser Gln Val Gln Ser Pro Phe Pro Ser Leu Cys Thr Leu

85

90

95

Val Glu Cys Leu Tyr Phe Val Ser Met Tyr Gly Ser Val Phe Thr Ile

100

105

110

Cys Phe Ile Ser Met Asp Arg Phe Leu Ala Ile Arg Tyr Pro Leu Leu

115

120

125

Val Ser His Leu Arg Ser Pro Arg Lys Ile Phe Gly Ile Cys Cys Thr

130

135

140

82/518

Ile Trp Val Leu Val Trp Thr Gly Ser Ile Pro Ile Tyr Ser Phe His  
 145                      150                      155                      160  
 Gly Lys Val Glu Lys Tyr Met Cys Phe His Asn Met Ser Asp Asp Thr  
                          165                      170                      175  
 Trp Ser Ala Lys Val Phe Phe Pro Leu Glu Val Phe Gly Phe Leu Leu  
                          180                      185                      190  
 Pro Met Gly Ile Met Gly Phe Cys Cys Ser Arg Ser Ile His Ile Leu  
                          195                      200                      205  
 Leu Gly Arg Arg Asp His Thr Gln Asp Trp Val Gln Gln Lys Ala Cys  
                          210                      215                      220  
 Ile Tyr Ser Ile Ala Ala Ser Leu Ala Val Phe Val Val Ser Phe Leu  
 225                      230                      235                      240  
 Pro Val His Leu Gly Phe Phe Leu Gln Phe Leu Val Arg Asn Ser Phe  
                          245                      250                      255  
 Ile Val Glu Cys Arg Ala Lys Gln Ser Ile Ser Phe Phe Leu Gln Leu  
                          260                      265                      270  
 Ser Met Cys Phe Ser Asn Val Asn Cys Cys Leu Asp Val Phe Cys Tyr  
                          275                      280                      285  
 Tyr Phe Val Ile Lys Glu Phe Arg Met Asn Ile Arg Ala His Arg Pro  
                          290                      295                      300  
 Ser Arg Val Gln Leu Val Leu Gln Asp Thr Thr Ile Ser Arg Gly Ala  
 305                      310                      315                      320  
 Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu  
                          325                      330                      335  
 Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly  
                          340                      345                      350  
 Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr  
                          355                      360                      365  
 Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys

83/518

370	375	380	
Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His			
385	390	395	400
Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr			
	405	410	415
Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys			
	420	425	430
Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp			
	435	440	445
Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr			
	450	455	460
Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile			
465	470	475	480
Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln			
	485	490	495
Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val			
	500	505	510
Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys			
	515	520	525
Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr			
	530	535	540
Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn			
545	550	555	

&lt;210&gt; 46

&lt;211&gt; 708

&lt;212&gt; PRT

&lt;213&gt; Human



84/518

&lt;400&gt; 46

Met Asp Thr Thr Met Glu Ala Asp Leu Gly Ala Thr Gly His Arg Pro

5

10

15

Arg Thr Glu Leu Asp Asp Glu Asp Ser Tyr Pro Gln Gly Gly Trp Asp

20

25

30

Thr Val Phe Leu Val Ala Leu Leu Leu Gly Leu Pro Ala Asn Gly

35

40

45

Leu Met Ala Trp Leu Ala Gly Ser Gln Ala Arg His Gly Ala Gly Thr

50

55

60

Arg Leu Ala Leu Leu Leu Ser Leu Ala Leu Ser Asp Phe Leu Phe

65

70

75

80

Leu Ala Ala Ala Phe Gln Ile Leu Glu Ile Arg His Gly Gly His

85

90

95

Trp Pro Leu Gly Thr Ala Ala Cys Arg Phe Tyr Tyr Phe Leu Trp Gly

100

105

110

Val Ser Tyr Ser Ser Gly Leu Phe Leu Leu Ala Ala Leu Ser Leu Asp

115

120

125

Arg Cys Leu Leu Ala Leu Cys Pro His Trp Tyr Pro Gly His Arg Pro

130

135

140

Val Arg Leu Pro Leu Trp Val Cys Ala Gly Val Trp Val Leu Ala Thr

145

150

155

160

Leu Phe Ser Val Pro Trp Leu Val Phe Pro Glu Ala Ala Val Trp Trp

165

170

175

Tyr Asp Leu Val Ile Cys Leu Asp Phe Trp Asp Ser Glu Glu Leu Ser

180

185

190

Leu Arg Met Leu Glu Val Leu Gly Gly Phe Leu Pro Phe Leu Leu Leu

195

200

205

Leu Val Cys His Val Leu Thr Gln Ala Thr Ala Cys Arg Thr Cys His

210

215

220

85/518

Arg Gln Gln Gln Pro Ala Ala Cys Arg Gly Phe Ala Arg Val Ala Arg  
 225                      230                      235                      240  
 Thr Ile Leu Ser Ala Tyr Val Val Leu Arg Leu Pro Tyr Gln Leu Ala  
                     245                      250                      255  
 Gln Leu Leu Tyr Leu Ala Phe Leu Trp Asp Val Tyr Ser Gly Tyr Leu  
                     260                      265                      270  
 Leu Trp Glu Ala Leu Val Tyr Ser Asp Tyr Leu Ile Leu Leu Asn Ser  
                     275                      280                      285  
 Cys Leu Ser Pro Phe Leu Cys Leu Met Ala Ser Ala Asp Leu Arg Thr  
                     290                      295                      300  
 Leu Leu Arg Ser Val Leu Ser Ser Phe Ala Ala Ala Leu Cys Glu Glu  
 305                      310                      315                      320  
 Arg Pro Gly Ser Phe Thr Pro Thr Glu Pro Gln Thr Gln Leu Asp Ser  
                     325                      330                      335  
 Glu Gly Pro Thr Leu Pro Glu Pro Met Ala Glu Ala Gln Ser Gln Met  
                     340                      345                      350  
 Asp Pro Val Ala Gln Pro Gln Val Asn Pro Thr Leu Gln Pro Arg Ser  
                     355                      360                      365  
 Asp Pro Thr Ala Gln Pro Gln Leu Asn Pro Thr Ala Gln Pro Gln Ser  
                     370                      375                      380  
 Asp Pro Thr Ala Gln Pro Gln Leu Asn Leu Met Ala Gln Pro Gln Ser  
 385                      390                      395                      400  
 Asp Ser Val Ala Gln Pro Gln Ala Asp Thr Asn Val Gln Thr Pro Ala  
                     405                      410                      415  
 Pro Ala Ala Ser Ser Val Pro Ser Pro Cys Asp Glu Ala Ser Pro Thr  
                     420                      425                      430  
 Pro Ser Ser His Pro Thr Pro Gly Ala Leu Glu Asp Pro Ala Thr Pro  
                     435                      440                      445  
 Pro Ala Ser Glu Gly Glu Ser Pro Ser Ser Thr Pro Pro Glu Ala Ala

86/518

450	455	460
Pro Gly Ala Gly Pro Thr Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly		
465	470	475 480
Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys		
485	490	495
Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu		
500	505	510
Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro		
515	520	525
Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr		
530	535	540
Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu		
545	550	555 560
Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr		
565	570	575
Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg		
580	585	590
Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly		
595	600	605
His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala		
610	615	620
Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn		
625	630	635 640
Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr		
645	650	655
Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser		
660	665	670
Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met		
675	680	685

87/518

Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp

690

695

700

Glu Leu Tyr Asn

705

&lt;210&gt; 47

&lt;211&gt; 637

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 47

Met Arg Pro Glu Arg Pro Arg Pro Arg Gly Ser Ala Pro Gly Pro Met

5

10

15

Glu Thr Pro Pro Trp Asp Pro Ala Arg Asn Asp Ser Leu Pro Pro Thr

20

25

30

Leu Thr Pro Ala Val Pro Pro Tyr Val Lys Leu Gly Leu Thr Val Val

35

40

45

Tyr Thr Val Phe Tyr Ala Leu Leu Phe Val Phe Ile Tyr Val Gln Leu

50

55

60

Trp Leu Val Leu Arg Tyr Arg His Lys Arg Leu Ser Tyr Gln Ser Val

65

70

75

80

Phe Leu Phe Leu Cys Leu Phe Trp Ala Ser Leu Arg Thr Val Leu Phe

85

90

95

Ser Phe Tyr Phe Lys Asp Phe Val Ala Ala Asn Ser Leu Ser Pro Phe

100

105

110

Val Phe Trp Leu Leu Tyr Cys Phe Pro Val Cys Leu Gln Phe Phe Thr

115

120

125

Leu Thr Leu Met Asn Leu Tyr Phe Thr Gln Val Ile Phe Lys Ala Lys

130

135

140

88/518

Ser Lys Tyr Ser Pro Glu Leu Leu Lys Tyr Arg Leu Pro Leu Tyr Leu  
 145 150 155 160  
 Ala Ser Leu Phe Ile Ser Leu Val Phe Leu Leu Val Asn Leu Thr Cys  
 165 170 175  
 Ala Val Leu Val Lys Thr Gly Asn Trp Glu Arg Lys Val Ile Val Ser  
 180 185 190  
 Val Arg Val Ala Ile Asn Asp Thr Leu Phe Val Leu Cys Ala Val Ser  
 195 200 205  
 Leu Ser Ile Cys Leu Tyr Lys Ile Ser Lys Met Ser Leu Ala Asn Ile  
 210 215 220  
 Tyr Leu Glu Ser Lys Gly Ser Ser Val Cys Gln Val Thr Ala Ile Gly  
 225 230 235 240  
 Val Thr Val Ile Leu Leu Tyr Thr Ser Arg Ala Cys Tyr Asn Leu Phe  
 245 250 255  
 Ile Leu Ser Phe Ser Gln Asn Lys Ser Val His Ser Phe Asp Tyr Asp  
 260 265 270  
 Trp Tyr Asn Val Ser Asp Gln Ala Asp Leu Lys Asn Gln Leu Gly Asp  
 275 280 285  
 Ala Gly Tyr Val Leu Phe Gly Val Val Leu Phe Val Trp Glu Leu Leu  
 290 295 300  
 Pro Thr Thr Leu Val Val Tyr Phe Phe Arg Val Arg Asn Pro Thr Lys  
 305 310 315 320  
 Asp Leu Thr Asn Pro Gly Met Val Pro Ser His Gly Phe Ser Pro Arg  
 325 330 335  
 Ser Tyr Phe Phe Asp Asn Pro Arg Arg Tyr Asp Ser Asp Asp Asp Leu  
 340 345 350  
 Ala Trp Asn Ile Ala Pro Gln Gly Leu Gln Gly Gly Phe Ala Pro Asp  
 355 360 365  
 Tyr Tyr Asp Trp Gly Gln Gln Thr Asn Ser Phe Leu Ala Gln Ala Gly

89/518

370	375	380	
Thr Leu Gln Asp Ser Thr Leu Asp Pro Asp Lys Pro Ser Leu Gly Ala			
385	390	395	400
Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu			
405	410	415	
Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly			
420	425	430	
Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr			
435	440	445	
Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys			
450	455	460	
Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His			
465	470	475	480
Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr			
485	490	495	
Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys			
500	505	510	
Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp			
515	520	525	
Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr			
530	535	540	
Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile			
545	550	555	560
Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln			
565	570	575	
Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val			
580	585	590	
Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys			
595	600	605	

90/518

Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr

610

615

620

Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn

625

630

635

&lt;210&gt; 48

&lt;211&gt; 657

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 48

Met Val Phe Ser Ala Val Leu Thr Ala Phe His Thr Gly Thr Ser Asn

5

10

15

Thr Thr Phe Val Val Tyr Glu Asn Thr Tyr Met Asn Ile Thr Leu Pro

20

25

30

Pro Pro Phe Gln His Pro Asp Leu Ser Pro Leu Leu Arg Tyr Ser Phe

35

40

45

Glu Thr Met Ala Pro Thr Gly Leu Ser Ser Leu Thr Val Asn Ser Thr

50

55

60

Ala Val Pro Thr Thr Pro Ala Ala Phe Lys Ser Leu Asn Leu Pro Leu

65

70

75

80

Gln Ile Thr Leu Ser Ala Ile Met Ile Phe Ile Leu Phe Val Ser Phe

85

90

95

Leu Gly Asn Leu Val Val Cys Leu Met Val Tyr Gln Lys Ala Ala Met

100

105

110

Arg Ser Ala Ile Asn Ile Leu Leu Ala Ser Leu Ala Phe Ala Asp Met

115

120

125

Leu Leu Ala Val Leu Asn Met Pro Phe Ala Leu Val Thr Ile Leu Thr

130

135

140

91/518

Thr Arg Trp Ile Phe Gly Lys Phe Phe Cys Arg Val Ser Ala Met Phe  
 145 150 155 160  
 Phe Trp Leu Phe Val Ile Glu Gly Val Ala Ile Leu Leu Ile Ile Ser  
 165 170 175  
 Ile Asp Arg Phe Leu Ile Ile Val Gln Arg Gln Asp Lys Leu Asn Pro  
 180 185 190  
 Tyr Arg Ala Lys Val Leu Ile Ala Val Ser Trp Ala Thr Ser Phe Cys  
 195 200 205  
 Val Ala Phe Pro Leu Ala Val Gly Asn Pro Asp Leu Gln Ile Pro Ser  
 210 215 220  
 Arg Ala Pro Gln Cys Val Phe Gly Tyr Thr Thr Asn Pro Gly Tyr Gln  
 225 230 235 240  
 Ala Tyr Val Ile Leu Ile Ser Leu Ile Ser Phe Phe Ile Pro Phe Leu  
 245 250 255  
 Val Ile Leu Tyr Ser Phe Met Gly Ile Leu Asn Thr Leu Arg His Asn  
 260 265 270  
 Ala Leu Arg Ile His Ser Tyr Pro Glu Gly Ile Cys Leu Ser Gln Ala  
 275 280 285  
 Ser Lys Leu Gly Leu Met Ser Leu Gln Arg Pro Phe Gln Met Ser Ile  
 290 295 300  
 Asp Met Gly Phe Lys Thr Arg Ala Phe Thr Thr Ile Leu Ile Leu Phe  
 305 310 315 320  
 Ala Val Phe Ile Val Cys Trp Ala Pro Phe Thr Thr Tyr Ser Leu Val  
 325 330 335  
 Ala Thr Phe Ser Lys His Phe Tyr Tyr Gln His Asn Phe Phe Glu Ile  
 340 345 350  
 Ser Thr Trp Leu Leu Trp Leu Cys Tyr Leu Lys Ser Ala Leu Asn Pro  
 355 360 365  
 Leu Ile Tyr Tyr Trp Arg Ile Lys Lys Phe His Asp Ala Cys Leu Asp



92/518

370	375	380	
Met Met Pro Lys Ser Phe Lys Phe Leu Pro Gln Leu Pro Gly His Thr			
385	390	395	400
Lys Arg Arg Ile Arg Pro Ser Ala Val Tyr Val Cys Gly Glu His Arg			
405	410	415	
Thr Val Val Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro			
420	425	430	
Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val			
435	440	445	
Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys			
450	455	460	
Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val			
465	470	475	480
Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His			
485	490	495	
Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val			
500	505	510	
Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg			
515	520	525	
Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu			
530	535	540	
Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu			
545	550	555	560
Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln			
565	570	575	
Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp			
580	585	590	
Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly			
595	600	605	

93/518

Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser  
 610 615 620  
 Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu  
 625 630 635 640  
 Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr  
 645 650 655  
 Asn

<210> 49  
 <211> 611  
 <212> PRT  
 <213> Human

<400> 49  
 Met Ala Asn Thr Thr Gly Glu Pro Glu Glu Val Ser Gly Ala Leu Ser  
 5 10 15  
 Pro Pro Ser Ala Ser Ala Tyr Val Lys Leu Val Leu Leu Gly Leu Ile  
 20 25 30  
 Met Cys Val Ser Leu Ala Gly Asn Ala Ile Leu Ser Leu Leu Val Leu  
 35 40 45  
 Lys Glu Arg Ala Leu His Lys Ala Pro Tyr Tyr Phe Leu Leu Asp Leu  
 50 55 60  
 Cys Leu Ala Asp Gly Ile Arg Ser Ala Val Cys Phe Pro Phe Val Leu  
 65 70 75 80  
 Ala Ser Val Arg His Gly Ser Ser Trp Thr Phe Ser Ala Leu Ser Cys  
 85 90 95  
 Lys Ile Val Ala Phe Met Ala Val Leu Phe Cys Phe His Ala Ala Phe  
 100 105 110  
 Met Leu Phe Cys Ile Ser Val Thr Arg Tyr Met Ala Ile Ala His His

94/518

115	120	125
Arg Phe Tyr Ala Lys Arg Met Thr Leu Trp Thr Cys Ala Ala Val Ile		
130	135	140
Cys Met Ala Trp Thr Leu Ser Val Ala Met Ala Phe Pro Pro Val Phe		
145	150	155
Asp Val Gly Thr Tyr Lys Phe Ile Arg Glu Glu Asp Gln Cys Ile Phe		
165	170	175
Glu His Arg Tyr Phe Lys Ala Asn Asp Thr Leu Gly Phe Met Leu Met		
180	185	190
Leu Ala Val Leu Met Ala Ala Thr His Ala Val Tyr Gly Lys Leu Leu		
195	200	205
Leu Phe Glu Tyr Arg His Arg Lys Met Lys Pro Val Gln Met Val Pro		
210	215	220
Ala Ile Ser Gln Asn Trp Thr Phe His Gly Pro Gly Ala Thr Gly Gln		
225	230	235
Ala Ala Ala Asn Trp Ile Ala Gly Phe Gly Arg Gly Pro Met Pro Pro		
245	250	255
Thr Leu Leu Gly Ile Arg Gln Asn Gly His Ala Ala Ser Arg Arg Leu		
260	265	270
Leu Gly Met Asp Glu Val Lys Gly Glu Lys Gln Leu Gly Arg Met Phe		
275	280	285
Tyr Ala Ile Thr Leu Leu Phe Leu Leu Leu Trp Ser Pro Tyr Ile Val		
290	295	300
Ala Cys Tyr Trp Arg Val Phe Val Lys Ala Cys Ala Val Pro His Arg		
305	310	315
Tyr Leu Ala Thr Ala Val Trp Met Ser Phe Ala Gln Ala Ala Val Asn		
325	330	335
Pro Ile Val Cys Phe Leu Leu Asn Lys Asp Leu Lys Lys Cys Leu Arg		
340	345	350

95/518

Thr His Ala Pro Cys Trp Gly Thr Gly Gly Ala Pro Ala Pro Arg Glu  
 355 360 365  
 Pro Tyr Cys Val Met Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val  
 370 375 380  
 Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe  
 385 390 395 400  
 Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr  
 405 410 415  
 Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr  
 420 425 430  
 Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro  
 435 440 445  
 Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly  
 450 455 460  
 Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys  
 465 470 475 480  
 Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile  
 485 490 495  
 Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His  
 500 505 510  
 Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp  
 515 520 525  
 Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile  
 530 535 540  
 Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro  
 545 550 555 560  
 Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr  
 565 570 575  
 Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val

96/518

580	585	590
Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu		
595	600	605
Leu Tyr Asn		
610		

<210> 50  
 <211> 798  
 <212> PRT  
 <213> Human

<400> 50

Met Asp Leu Lys Thr Val Leu Ser Leu Pro Arg Tyr Pro Gly Glu Phe  
5 10 15  
Leu His Pro Val Val Tyr Ala Cys Thr Ala Val Met Leu Leu Cys Leu  
20 25 30  
Leu Ala Ser Phe Val Thr Tyr Ile Val His Gln Ser Ala Ile Arg Ile  
35 40 45  
Ser Arg Lys Gly Arg His Thr Leu Leu Asn Phe Cys Phe His Ala Ala  
50 55 60  
Leu Thr Phe Thr Val Phe Ala Gly Gly Ile Asn Arg Thr Lys Tyr Pro  
65 70 75 80  
Ile Leu Cys Gln Ala Val Gly Ile Val Leu His Tyr Ser Thr Leu Ser  
85 90 95  
Thr Met Leu Trp Ile Gly Val Thr Ala Arg Asn Ile Tyr Lys Gln Val  
100 105 110  
Thr Lys Lys Ala Pro Leu Cys Leu Asp Thr Asp Gln Pro Pro Tyr Pro  
115 120 125  
Arg Gln Pro Leu Leu Arg Phe Tyr Leu Val Ser Gly Gly Val Pro Phe

97/518

130	135	140	
Ile Ile Cys Gly Val Thr Ala Ala Thr Asn Ile Arg Asn Tyr Gly Thr			
145	150	155	160
Glu Asp Glu Asp Thr Ala Tyr Cys Trp Met Ala Trp Glu Pro Ser Leu			
	165	170	175
Gly Ala Phe Tyr Gly Pro Ala Ala Ile Ile Thr Leu Val Thr Cys Val			
	180	185	190
Tyr Phe Leu Gly Thr Tyr Val Gln Leu Arg Arg His Pro Gly Arg Arg			
	195	200	205
Tyr Glu Leu Arg Thr Gln Pro Glu Glu Gln Arg Arg Leu Ala Thr Pro			
	210	215	220
Glu Gly Gly Arg Gly Ile Arg Pro Gly Thr Pro Pro Ala His Asp Ala			
225	230	235	240
Pro Gly Ala Ser Val Leu Gln Asn Glu His Ser Phe Gln Ala Gln Leu			
	245	250	255
Arg Ala Ala Ala Phe Thr Leu Phe Leu Phe Thr Ala Thr Trp Ala Phe			
	260	265	270
Gly Ala Leu Ala Val Ser Gln Gly His Phe Leu Asp Met Val Phe Ser			
	275	280	285
Cys Leu Tyr Gly Ala Phe Cys Val Thr Leu Gly Leu Phe Val Leu Ile			
	290	295	300
His His Cys Ala Lys Arg Glu Asp Val Trp Gln Cys Trp Trp Ala Cys			
305	310	315	320
Cys Pro Pro Arg Lys Asp Ala His Pro Ala Leu Asp Ala Asn Gly Ala			
	325	330	335
Ala Leu Gly Arg Ala Ala Cys Leu His Ser Pro Gly Leu Gly Gln Pro			
	340	345	350
Arg Gly Phe Ala His Pro Pro Gly Pro Cys Lys Met Thr Asn Leu Gln			
	355	360	365

98/518

Ala Ala Gln Gly His Ala Ser Cys Leu Ser Pro Ala Thr Pro Cys Cys  
 370 375 380  
 Ala Lys Met His Cys Glu Pro Leu Thr Ala Asp Glu Ala His Val His  
 385 390 395 400  
 Leu Gln Glu Glu Gly Ala Phe Gly His Asp Pro His Leu His Gly Cys  
 405 410 415  
 Leu Gln Gly Arg Thr Lys Pro Pro Tyr Phe Ser Arg His Pro Ala Glu  
 420 425 430  
 Glu Pro Glu Tyr Ala Tyr His Ile Pro Ser Ser Leu Asp Gly Ser Pro  
 435 440 445  
 Arg Ser Ser Arg Thr Asp Ser Pro Pro Ser Ser Leu Asp Gly Pro Ala  
 450 455 460  
 Gly Thr His Thr Leu Ala Cys Cys Thr Gln Gly Asp Pro Phe Pro Met  
 465 470 475 480  
 Val Thr Gln Pro Glu Gly Ser Asp Gly Ser Pro Ala Leu Tyr Ser Cys  
 485 490 495  
 Pro Thr Gln Pro Gly Arg Glu Ala Ala Leu Gly Pro Gly His Leu Glu  
 500 505 510  
 Met Leu Arg Arg Thr Gln Ser Leu Pro Phe Gly Gly Pro Ser Gln Asn  
 515 520 525  
 Gly Leu Pro Lys Gly Lys Leu Leu Glu Gly Leu Pro Phe Gly Thr Asp  
 530 535 540  
 Gly Thr Gly Asn Ile Arg Thr Gly Pro Trp Lys Asn Glu Thr Thr Val  
 545 550 555 560  
 Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val  
 565 570 575  
 Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu  
 580 585 590  
 Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys

99/518

595	600	605
Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu		
610	615	620
Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg		
625	630	635
His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg		
645	650	655
Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val		
660	665	670
Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile		
675	680	685
Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn		
690	695	700
Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly		
705	710	715
Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val		
725	730	735
Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro		
740	745	750
Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser		
755	760	765
Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val		
770	775	780
Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn		
785	790	795

&lt;210&gt; 51

&lt;211&gt; 557

&lt;212&gt; PRT



100/518

&lt;213&gt; Human

&lt;400&gt; 51

Met Thr Asn Ser Ser Phe Phe Cys Pro Val Tyr Lys Asp Leu Glu Pro  
                     5                    10                    15  
 Phe Thr Tyr Phe Phe Tyr Leu Val Phe Leu Val Gly Ile Ile Gly Ser  
                     20                    25                    30  
 Cys Phe Ala Thr Trp Ala Phe Ile Gln Lys Asn Thr Asn His Arg Cys  
                     35                    40                    45  
 Val Ser Ile Tyr Leu Ile Asn Leu Leu Thr Ala Asp Phe Leu Leu Thr  
                     50                    55                    60  
 Leu Ala Leu Pro Val Lys Ile Val Val Asp Leu Gly Val Ala Pro Trp  
                     65                    70                    75                    80  
 Lys Leu Lys Ile Phe His Cys Gln Val Thr Ala Cys Leu Ile Tyr Ile  
                     85                    90                    95  
 Asn Met Tyr Leu Ser Ile Ile Phe Leu Ala Phe Val Ser Ile Asp Arg  
                     100                    105                    110  
 Cys Leu Gln Leu Thr His Ser Cys Lys Ile Tyr Arg Ile Gln Glu Pro  
                     115                    120                    125  
 Gly Phe Ala Lys Met Ile Ser Thr Val Val Trp Leu Met Val Leu Leu  
                     130                    135                    140  
 Ile Met Val Pro Asn Met Met Ile Pro Ile Lys Asp Ile Lys Glu Lys  
                     145                    150                    155                    160  
 Ser Asn Val Gly Cys Met Glu Phe Lys Lys Glu Phe Gly Arg Asn Trp  
                     165                    170                    175  
 His Leu Leu Thr Asn Phe Ile Cys Val Ala Ile Phe Leu Asn Phe Ser  
                     180                    185                    190  
 Ala Ile Ile Leu Ile Ser Asn Cys Leu Val Ile Arg Gln Leu Tyr Arg  
                     195                    200                    205

101/518

Asn Lys Asp Asn Glu Asn Tyr Pro Asn Val Lys Lys Ala Leu Ile Asn			
210	215	220	
Ile Leu Leu Val Thr Thr Gly Tyr Ile Ile Cys Phe Val Pro Tyr His			
225	230	235	240
Ile Val Arg Ile Pro Tyr Thr Leu Ser Gln Thr Glu Val Ile Thr Asp			
	245	250	255
Cys Ser Thr Arg Ile Ser Leu Phe Lys Ala Lys Glu Ala Thr Leu Leu			
	260	265	270
Leu Ala Val Ser Asn Leu Cys Phe Asp Pro Ile Leu Tyr Tyr His Leu			
	275	280	285
Ser Lys Ala Phe Arg Ser Lys Val Thr Glu Thr Phe Ala Ser Pro Lys			
	290	295	300
Glu Thr Lys Ala Gln Lys Glu Lys Leu Arg Cys Glu Asn Asn Ala Ala			
305	310	315	320
Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu			
	325	330	335
Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly			
	340	345	350
Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr			
	355	360	365
Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys			
	370	375	380
Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His			
385	390	395	400
Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr			
	405	410	415
Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys			
	420	425	430
Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp			

102/518

435                      440                      445  
 Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr  
 450                      455                      460  
 Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile  
 465                      470                      475                      480  
 Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln  
                          485                      490                      495  
 Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val  
                          500                      505                      510  
 Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys  
                          515                      520                      525  
 Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr  
                          530                      535                      540  
 Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
 545                      550                      555

&lt;210&gt; 52

&lt;211&gt; 596

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 52

Met Gly Phe Asn Leu Thr Leu Ala Lys Leu Pro Asn Asn Glu Leu His  
                          5                      10                      15  
 Gly Gln Glu Ser His Asn Ser Gly Asn Arg Ser Asp Gly Pro Gly Lys  
                          20                      25                      30  
 Asn Thr Thr Leu His Asn Glu Phe Asp Thr Ile Val Leu Pro Val Leu  
                          35                      40                      45  
 Tyr Leu Ile Ile Phe Val Ala Ser Ile Leu Leu Asn Gly Leu Ala Val

103/518

50	55	60	
Trp Ile Phe Phe His Ile Arg Asn Lys Thr Ser Phe Ile Phe Tyr Leu			
65	70	75	80
Lys Asn Ile Val Val Ala Asp Leu Ile Met Thr Leu Thr Phe Pro Phe			
85	90	95	
Arg Ile Val His Asp Ala Gly Phe Gly Pro Trp Tyr Phe Lys Phe Ile			
100	105	110	
Leu Cys Arg Tyr Thr Ser Val Leu Phe Tyr Ala Asn Met Tyr Thr Ser			
115	120	125	
Ile Val Phe Leu Gly Leu Ile Ser Ile Asp Arg Tyr Leu Lys Val Val			
130	135	140	
Lys Pro Phe Gly Asp Ser Arg Met Tyr Ser Ile Thr Phe Thr Lys Val			
145	150	155	160
Leu Ser Val Cys Val Trp Val Ile Met Ala Val Leu Ser Leu Pro Asn			
165	170	175	
Ile Ile Leu Thr Asn Gly Gln Pro Thr Glu Asp Asn Ile His Asp Cys			
180	185	190	
Ser Lys Leu Lys Ser Pro Leu Gly Val Lys Trp His Thr Ala Val Thr			
195	200	205	
Tyr Val Asn Ser Cys Leu Phe Val Ala Val Leu Val Ile Leu Ile Gly			
210	215	220	
Cys Tyr Ile Ala Ile Ser Arg Tyr Ile His Lys Ser Ser Arg Gln Phe			
225	230	235	240
Ile Ser Gln Ser Ser Arg Lys Arg Lys His Asn Gln Ser Ile Arg Val			
245	250	255	
Val Val Ala Val Phe Phe Thr Cys Phe Leu Pro Tyr His Leu Cys Arg			
260	265	270	
Ile Pro Phe Thr Phe Ser His Leu Asp Arg Leu Leu Asp Glu Ser Ala			
275	280	285	

104/518

Gln Lys Ile Leu Tyr Tyr Cys Lys Glu Ile Thr Leu Phe Leu Ser Ala  
 290 295 300  
 Cys Asn Val Cys Leu Asp Pro Ile Ile Tyr Phe Phe Met Cys Arg Ser  
 305 310 315 320  
 Phe Ser Arg Arg Leu Phe Lys Lys Ser Asn Ile Arg Thr Arg Ser Glu  
 325 330 335  
 Ser Ile Arg Ser Leu Gln Ser Val Arg Arg Ser Glu Val Arg Ile Tyr  
 340 345 350  
 Tyr Asp Tyr Thr Asp Val Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly  
 355 360 365  
 Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys  
 370 375 380  
 Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu  
 385 390 395 400  
 Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro  
 405 410 415  
 Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr  
 420 425 430  
 Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu  
 435 440 445  
 Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr  
 450 455 460  
 Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg  
 465 470 475 480  
 Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly  
 485 490 495  
 His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala  
 500 505 510  
 Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn

105/518

515                      520                      525  
 Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr  
 530                      535                      540  
 Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser  
 545                      550                      555                      560  
 Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met  
 565                      570                      575  
 Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp  
 580                      585                      590  
 Glu Leu Tyr Asn  
 595

&lt;210&gt; 53

&lt;211&gt; 572

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 53

Met Leu Gly Ile Met Ala Trp Asn Ala Thr Cys Lys Asn Trp Leu Ala  
                                  5                                   10                                   15  
 Ala Glu Ala Ala Leu Glu Lys Tyr Tyr Leu Ser Ile Phe Tyr Gly Ile  
                                  20                                   25                                   30  
 Glu Phe Val Val Gly Val Leu Gly Asn Thr Ile Val Val Tyr Gly Tyr  
                                  35                                   40                                   45  
 Ile Phe Ser Leu Lys Asn Trp Asn Ser Ser Asn Ile Tyr Leu Phe Asn  
                                  50                                   55                                   60  
 Leu Ser Val Ser Asp Leu Ala Phe Leu Cys Thr Leu Pro Met Leu Ile  
                                  65                                   70                                   75                                   80  
 Arg Ser Tyr Ala Asn Gly Asn Trp Ile Tyr Gly Asp Val Leu Cys Ile

106/518

	85		90		95
Ser Asn Arg Tyr Val Leu His Ala Asn Leu Tyr Thr Ser Ile Leu Phe					
	100		105		110
Leu Thr Phe Ile Ser Ile Asp Arg Tyr Leu Ile Ile Lys Tyr Pro Phe					
	115		120		125
Arg Glu His Leu Leu Gln Lys Lys Glu Phe Ala Ile Leu Ile Ser Leu					
	130		135		140
Ala Ile Trp Val Leu Val Thr Leu Glu Leu Leu Pro Ile Leu Pro Leu					
	145		150		155
Ile Asn Pro Val Ile Thr Asp Asn Gly Thr Thr Cys Asn Asp Phe Ala					
	165		170		175
Ser Ser Gly Asp Pro Asn Tyr Asn Leu Ile Tyr Ser Met Cys Leu Thr					
	180		185		190
Leu Leu Gly Phe Leu Ile Pro Leu Phe Val Met Cys Phe Phe Tyr Tyr					
	195		200		205
Lys Ile Ala Leu Phe Leu Lys Gln Arg Asn Arg Gln Val Ala Thr Ala					
	210		215		220
Leu Pro Leu Glu Lys Pro Leu Asn Leu Val Ile Met Ala Val Val Ile					
	225		230		235
Phe Ser Val Pro Phe Thr Pro Tyr His Val Met Arg Asn Val Arg Ile					
	245		250		255
Ala Ser Arg Leu Gly Ser Trp Lys Gln Tyr Gln Cys Thr Gln Val Val					
	260		265		270
Ile Asn Ser Phe Tyr Ile Val Thr Arg Pro Leu Ala Phe Leu Asn Ser					
	275		280		285
Val Ile Asn Pro Val Phe Tyr Phe Leu Leu Gly Asp His Phe Arg Asp					
	290		295		300
Met Leu Met Asn Gln Leu Arg His Asn Phe Lys Ser Leu Thr Ser Phe					
	305		310		315
					320

Ser	Arg	Trp	Ala	His	Glu	Leu	Leu	Leu	Ser	Phe	Arg	Glu	Lys	Ala	Ser		
325					330					335							
Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu	Val	Glu	Leu		
340					345					350							
Asp	Gly	Asp	Val	Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly	Glu	Gly	Glu		
355					360					365							
Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile	Cys	Thr	Thr		
370					375					380							
Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr	Leu	Cys	Tyr		
385					390					395						400	
Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys	Arg	His	Asp		
405					410					415							
Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu	Arg	Thr	Ile		
420					425					430							
Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	Val	Lys	Phe		
435					440					445							
Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly	Ile	Asp	Phe		
450					455					460							
Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	Asn	Tyr	Asn		
465					470					475						480	
Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	Gly	Ile	Lys		
485					490					495							
Val	Asn	Phe	Lys	Thr	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser	Val	Gln	Leu		
500					505					510							
Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly	Pro	Val	Leu		
515					520					525							
Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu	Ser	Lys	Asp		
530					535					540							
Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe	Val	Thr	Ala		



108/518

545                      550                      555                      560  
 Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
                          565                      570

&lt;210&gt; 54

&lt;211&gt; 575

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 54

Met Arg Ala Val Phe Ile Gln Gly Ala Glu Glu His Pro Ala Ala Phe  
                          5                      10                      15  
 Cys Tyr Gln Val Asn Gly Ser Cys Pro Arg Thr Val His Thr Leu Gly  
                          20                      25                      30  
 Ile Gln Leu Val Ile Tyr Leu Ala Cys Ala Ala Gly Met Leu Ile Ile  
                          35                      40                      45  
 Val Leu Gly Asn Val Phe Val Ala Phe Ala Val Ser Tyr Phe Lys Ala  
                          50                      55                      60  
 Leu His Thr Pro Thr Asn Phe Leu Leu Leu Ser Leu Ala Leu Ala Asp  
                          65                      70                      75                      80  
 Met Phe Leu Gly Leu Leu Val Leu Pro Leu Ser Thr Ile Arg Ser Val  
                          85                      90                      95  
 Glu Ser Cys Trp Phe Phe Gly Asp Phe Leu Cys Arg Leu His Thr Tyr  
                          100                      105                      110  
 Leu Asp Thr Leu Phe Cys Leu Thr Ser Ile Phe His Leu Cys Phe Ile  
                          115                      120                      125  
 Ser Ile Asp Arg His Cys Ala Ile Cys Asp Pro Leu Leu Tyr Pro Ser  
                          130                      135                      140  
 Lys Phe Thr Val Arg Val Ala Leu Arg Tyr Ile Leu Ala Gly Trp Gly

109/518

145	150	155	160
Val Pro Ala Ala Tyr Thr Ser Leu Phe Leu Tyr Thr Asp Val Val Glu			
	165	170	175
Thr Arg Leu Ser Gln Trp Leu Glu Glu Met Pro Cys Val Gly Ser Cys			
	180	185	190
Gln Leu Leu Leu Asn Lys Phe Trp Gly Trp Leu Asn Phe Pro Leu Phe			
	195	200	205
Phe Val Pro Cys Leu Ile Met Ile Ser Leu Tyr Val Lys Ile Phe Val			
	210	215	220
Val Ala Thr Arg Gln Ala Gln Gln Ile Thr Thr Leu Ser Lys Ser Leu			
225	230	235	240
Ala Gly Ala Ala Lys His Glu Arg Lys Ala Ala Lys Thr Leu Gly Ile			
	245	250	255
Ala Val Gly Ile Tyr Leu Leu Cys Trp Leu Pro Phe Thr Ile Asp Thr			
	260	265	270
Met Val Asp Ser Leu Leu His Phe Ile Thr Pro Pro Leu Val Phe Asp			
	275	280	285
Ile Phe Ile Trp Phe Ala Tyr Phe Asn Ser Ala Cys Asn Pro Ile Ile			
	290	295	300
Tyr Val Phe Ser Tyr Gln Trp Phe Arg Lys Ala Leu Lys Leu Thr Leu			
305	310	315	320
Ser Gln Lys Val Phe Ser Pro Gln Thr Arg Thr Val Asp Leu Tyr Gln			
	325	330	335
Glu Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu			
	340	345	350
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly			
	355	360	365
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile			
	370	375	380

110/518

Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr  
 385                      390                      395                      400  
 Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys  
                     405                      410                      415  
 Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu  
                     420                      425                      430  
 Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu  
                     435                      440                      445  
 Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly  
                     450                      455                      460  
 Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr  
 465                      470                      475                      480  
 Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn  
                     485                      490                      495  
 Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser  
                     500                      505                      510  
 Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly  
                     515                      520                      525  
 Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu  
                     530                      535                      540  
 Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe  
 545                      550                      555                      560  
 Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
                     565                      570                      575

&lt;210&gt; 55

&lt;211&gt; 580

&lt;212&gt; PRT

&lt;213&gt; Human

111/518

&lt;400&gt; 55

Met Thr Ser Asn Phe Ser Gln Pro Val Val Gln Leu Cys Tyr Glu Asp  
                           5                          10                          15  
 Val Asn Gly Ser Cys Ile Glu Thr Pro Tyr Ser Pro Gly Ser Arg Val  
                           20                          25                          30  
 Ile Leu Tyr Thr Ala Phe Ser Phe Gly Ser Leu Leu Ala Val Phe Gly  
                           35                          40                          45  
 Asn Leu Leu Val Met Thr Ser Val Leu His Phe Lys Gln Leu His Ser  
                           50                          55                          60  
 Pro Thr Asn Phe Leu Ile Ala Ser Leu Ala Cys Ala Asp Phe Leu Val  
                           65                          70                          75                          80  
 Gly Val Thr Val Met Leu Phe Ser Met Val Arg Thr Val Glu Ser Cys  
                           85                          90                          95  
 Trp Tyr Phe Gly Ala Lys Phe Cys Thr Leu His Ser Cys Cys Asp Val  
                           100                          105                          110  
 Ala Phe Cys Tyr Ser Ser Val Leu His Leu Cys Phe Ile Cys Ile Asp  
                           115                          120                          125  
 Arg Tyr Ile Val Val Thr Asp Pro Leu Val Tyr Ala Thr Lys Phe Thr  
                           130                          135                          140  
 Val Ser Val Ser Gly Ile Cys Ile Ser Val Ser Trp Ile Leu Pro Leu  
                           145                          150                          155                          160  
 Thr Tyr Ser Gly Ala Val Phe Tyr Thr Gly Val Asn Asp Asp Gly Leu  
                           165                          170                          175  
 Glu Glu Leu Val Ser Ala Leu Asn Cys Val Gly Gly Cys Gln Ile Ile  
                           180                          185                          190  
 Val Ser Gln Gly Trp Val Leu Ile Asp Phe Leu Leu Phe Phe Ile Pro  
                           195                          200                          205  
 Thr Leu Val Met Ile Ile Leu Tyr Ser Lys Ile Phe Leu Ile Ala Lys

112/518

210	215	220
Gln Gln Ala Ile Lys Ile Glu Thr Thr Ser Ser Lys Val Glu Ser Ser		
225	230	235
Ser Glu Ser Tyr Lys Ile Arg Val Ala Lys Arg Glu Arg Lys Ala Ala		240
245	250	255
Lys Thr Leu Gly Val Thr Val Leu Ala Phe Val Ile Ser Trp Leu Pro		
260	265	270
Tyr Thr Val Asp Ile Leu Ile Asp Ala Phe Met Gly Phe Leu Thr Pro		
275	280	285
Ala Tyr Ile Tyr Glu Ile Cys Cys Trp Ser Ala Tyr Tyr Asn Ser Ala		
290	295	300
Met Asn Pro Leu Ile Tyr Ala Leu Phe Tyr Pro Trp Phe Arg Lys Ala		
305	310	315
Ile Lys Leu Ile Leu Ser Gly Asp Val Leu Lys Ala Ser Ser Ser Thr		320
325	330	335
Ile Ser Leu Phe Leu Glu Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly		
340	345	350
Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys		
355	360	365
Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu		
370	375	380
Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro		
385	390	395
Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr		400
405	410	415
Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu		
420	425	430
Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr		
435	440	445

113/518

Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg  
 450 455 460  
 Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly  
 465 470 475 480  
 His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala  
 485 490 495  
 Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn  
 500 505 510  
 Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr  
 515 520 525  
 Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser  
 530 535 540  
 Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met  
 545 550 555 560  
 Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp  
 565 570 575  
 Glu Leu Tyr Asn  
 580

&lt;210&gt; 56

&lt;211&gt; 583

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 56

Met Ser Ser Asn Ser Ser Leu Leu Val Ala Val Gln Leu Cys Tyr Ala  
 5 10 15  
 Asn Val Asn Gly Ser Cys Val Lys Ile Pro Phe Ser Pro Gly Ser Arg  
 20 25 30

114/518

Val Ile Leu Tyr Ile Val Phe Gly Phe Gly Ala Val Leu Ala Val Phe  
 35 40 45  
 Gly Asn Leu Leu Val Met Ile Ser Ile Leu His Phe Lys Gln Leu His  
 50 55 60  
 Ser Pro Thr Asn Phe Leu Val Ala Ser Leu Ala Cys Ala Asp Phe Leu  
 65 70 75 80  
 Val Gly Val Thr Val Met Pro Phe Ser Met Val Arg Thr Val Glu Ser  
 85 90 95  
 Cys Trp Tyr Phe Gly Arg Ser Phe Cys Thr Phe His Thr Cys Cys Asp  
 100 105 110  
 Val Ala Phe Cys Tyr Ser Ser Leu Phe His Leu Cys Phe Ile Ser Ile  
 115 120 125  
 Asp Arg Tyr Ile Ala Val Thr Asp Pro Leu Val Tyr Pro Thr Lys Phe  
 130 135 140  
 Thr Val Ser Val Ser Gly Ile Cys Ile Ser Val Ser Trp Ile Leu Pro  
 145 150 155 160  
 Leu Met Tyr Ser Gly Ala Val Phe Tyr Thr Gly Val Tyr Asp Asp Gly  
 165 170 175  
 Leu Glu Glu Leu Ser Asp Ala Leu Asn Cys Ile Gly Gly Cys Gln Thr  
 180 185 190  
 Val Val Asn Gln Asn Trp Val Leu Thr Asp Phe Leu Ser Phe Phe Ile  
 195 200 205  
 Pro Thr Phe Ile Met Ile Ile Leu Tyr Gly Asn Ile Phe Leu Val Ala  
 210 215 220  
 Arg Arg Gln Ala Lys Lys Ile Glu Asn Thr Gly Ser Lys Thr Glu Ser  
 225 230 235 240  
 Ser Ser Glu Ser Tyr Lys Ala Arg Val Ala Arg Arg Glu Arg Lys Ala  
 245 250 255  
 Ala Lys Thr Leu Gly Val Thr Val Val Ala Phe Met Ile Ser Trp Leu

115/518

260	265	270
Pro Tyr Ser Ile Asp Ser Leu Ile Asp Ala Phe Met Gly Phe Ile Thr		
275	280	285
Pro Ala Cys Ile Tyr Glu Ile Cys Cys Trp Cys Ala Tyr Tyr Asn Ser		
290	295	300
Ala Met Asn Pro Leu Ile Tyr Ala Leu Phe Tyr Pro Trp Phe Arg Lys		
305	310	315
Ala Ile Lys Val Ile Val Thr Gly Gln Val Leu Lys Asn Ser Ser Ala		
325	330	335
Thr Met Asn Leu Phe Ser Glu His Ile Ala Ser Lys Gly Glu Glu Leu		
340	345	350
Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn		
355	360	365
Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr		
370	375	380
Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val		
385	390	395
Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe		
405	410	415
Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala		
420	425	430
Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp		
435	440	445
Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu		
450	455	460
Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn		
465	470	475
Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr		
485	490	495



116/518

Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr  
                   500                  505                  510  
 Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln  
                   515                  520                  525  
 Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His  
                   530                  535                  540  
 Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg  
                   545                  550                  555                  560  
 Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His  
                   565                  570                  575  
 Gly Met Asp Glu Leu Tyr Asn  
                   580

&lt;210&gt; 57

&lt;211&gt; 851

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 57

Met Gly Pro Thr Leu Ala Val Pro Thr Pro Tyr Gly Cys Ile Gly Cys  
                   5                  10                  15  
 Lys Leu Pro Gln Pro Glu Tyr Pro Pro Ala Leu Ile Ile Phe Met Phe  
                   20                  25                  30  
 Cys Ala Met Val Ile Thr Ile Val Val Asp Leu Ile Gly Asn Ser Met  
                   35                  40                  45  
 Val Ile Leu Ala Val Thr Lys Asn Lys Lys Leu Arg Asn Ser Gly Asn  
                   50                  55                  60  
 Ile Phe Val Val Ser Leu Ser Val Ala Asp Met Leu Val Ala Ile Tyr  
                   65                  70                  75                  80

117/518

Pro Tyr Pro Leu Met Leu His Ala Met Ser Ile Gly Gly Trp Asp Leu  
                     85                    90                    95  
 Ser Gln Leu Gln Cys Gln Met Val Gly Phe Ile Thr Gly Leu Ser Val  
                     100                    105                    110  
 Val Gly Ser Ile Phe Asn Ile Val Ala Ile Ala Ile Asn Arg Tyr Cys  
                     115                    120                    125  
 Tyr Ile Cys His Ser Leu Gln Tyr Glu Arg Ile Phe Ser Val Arg Asn  
                     130                    135                    140  
 Thr Cys Ile Tyr Leu Val Ile Thr Trp Ile Met Thr Val Leu Ala Val  
 145                    150                    155                    160  
 Leu Pro Asn Met Tyr Ile Gly Thr Ile Glu Tyr Asp Pro Arg Thr Tyr  
                     165                    170                    175  
 Thr Cys Ile Phe Asn Tyr Leu Asn Asn Pro Val Phe Thr Val Thr Ile  
                     180                    185                    190  
 Val Cys Ile His Phe Val Leu Pro Leu Leu Ile Val Gly Phe Cys Tyr  
                     195                    200                    205  
 Val Arg Ile Trp Thr Lys Val Leu Ala Ala Arg Asp Pro Ala Gly Gln  
                     210                    215                    220  
 Asn Pro Asp Asn Gln Leu Ala Glu Val Arg Asn Phe Leu Thr Met Phe  
 225                    230                    235                    240  
 Val Ile Phe Leu Leu Phe Ala Val Cys Trp Cys Pro Ile Asn Val Leu  
                     245                    250                    255  
 Thr Val Leu Val Ala Val Ser Pro Lys Glu Met Ala Gly Lys Ile Pro  
                     260                    265                    270  
 Asn Trp Leu Tyr Leu Ala Ala Tyr Phe Ile Ala Tyr Phe Asn Ser Cys  
                     275                    280                    285  
 Leu Asn Ala Val Ile Tyr Gly Leu Leu Asn Glu Asn Phe Arg Arg Glu  
                     290                    295                    300  
 Tyr Trp Thr Ile Phe His Ala Met Arg His Pro Ile Ile Phe Phe Pro

118/518

305	310	315	320
Gly Leu Ile Ser Asp Ile Arg Glu Met Gln Glu Ala Arg Thr Leu Ala			
325	330	335	
Arg Ala Arg Ala His Ala Arg Asp Gln Ala Arg Glu Gln Asp Arg Ala			
340	345	350	
His Ala Cys Pro Ala Val Glu Glu Thr Pro Met Asn Val Arg Asn Val			
355	360	365	
Pro Leu Pro Gly Asp Ala Ala Ala Gly His Pro Asp Arg Ala Ser Gly			
370	375	380	
His Pro Lys Pro His Ser Arg Ser Ser Ser Ala Tyr Arg Lys Ser Ala			
385	390	395	400
Ser Thr His His Lys Ser Val Phe Ser His Ser Lys Ala Ala Ser Gly			
405	410	415	
His Leu Lys Pro Val Ser Gly His Ser Lys Pro Ala Ser Gly His Pro			
420	425	430	
Lys Ser Ala Thr Val Tyr Pro Lys Pro Ala Ser Val His Phe Lys Gly			
435	440	445	
Asp Ser Val His Phe Lys Gly Asp Ser Val His Phe Lys Pro Asp Ser			
450	455	460	
Val His Phe Lys Pro Ala Ser Ser Asn Pro Lys Pro Ile Thr Gly His			
465	470	475	480
His Val Ser Ala Gly Ser His Ser Lys Ser Ala Phe Ser Ala Ala Thr			
485	490	495	
Ser His Pro Lys Pro Ile Lys Pro Ala Thr Ser His Ala Glu Pro Thr			
500	505	510	
Thr Ala Asp Tyr Pro Lys Pro Ala Thr Thr Ser His Pro Lys Pro Ala			
515	520	525	
Ala Ala Asp Asn Pro Glu Leu Ser Ala Ser His Cys Pro Glu Ile Pro			
530	535	540	

119/518

Ala Ile Ala His Pro Val Ser Asp Asp Ser Asp Leu Pro Glu Ser Ala  
 545                      550                      555                      560  
 Ser Ser Pro Ala Ala Gly Pro Thr Lys Pro Ala Ala Ser Gln Leu Glu  
                          565                      570                      575  
 Ser Asp Thr Ile Ala Asp Leu Pro Asp Pro Thr Val Val Thr Thr Ser  
                          580                      585                      590  
 Thr Asn Asp Tyr His Asp Val Val Val Asp Val Glu Asp Asp Pro  
                          595                      600                      605  
 Asp Glu Met Ala Val Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val  
                          610                      615                      620  
 Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe  
 625                      630                      635                      640  
 Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr  
                          645                      650                      655  
 Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr  
                          660                      665                      670  
 Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro  
                          675                      680                      685  
 Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly  
                          690                      695                      700  
 Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys  
 705                      710                      715                      720  
 Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile  
                          725                      730                      735  
 Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His  
                          740                      745                      750  
 Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp  
                          755                      760                      765  
 Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile

120/518

770                      775                      780  
 Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro  
 785                      790                      795                      800  
 Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr  
                     805                      810                      815  
 Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val  
                     820                      825                      830  
 Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu  
                     835                      840                      845  
 Leu Tyr Asn  
                     850

&lt;210&gt; 58

&lt;211&gt; 895

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 58

Met Lys Met Lys Ser Gln Ala Thr Met Ile Cys Cys Leu Val Phe Phe  
                     5                      10                      15  
 Leu Ser Thr Glu Cys Ser His Tyr Arg Ser Lys Ile His Leu Lys Ala  
                     20                      25                      30  
 Gly Asp Lys Leu Gln Ser Pro Glu Gly Lys Pro Lys Thr Gly Arg Ile  
                     35                      40                      45  
 Gln Glu Lys Cys Glu Gly Pro Cys Ile Ser Ser Ser Asn Cys Ser Gln  
                     50                      55                      60  
 Pro Cys Ala Lys Asp Phe His Gly Glu Ile Gly Phe Thr Cys Asn Gln  
                     65                      70                      75                      80  
 Lys Lys Trp Gln Lys Ser Ala Glu Thr Cys Thr Ser Leu Ser Val Glu

121/518

	85		90		95										
Lys	Leu	Phe	Lys	Asp	Ser	Thr	Gly	Ala	Ser	Arg	Leu	Ser	Val	Ala	Ala
	100						105						110		
Pro	Ser	Ile	Pro	Leu	His	Ile	Leu	Asp	Phe	Arg	Ala	Pro	Glu	Thr	Ile
	115						120						125		
Glu	Ser	Val	Ala	Gln	Gly	Ile	Arg	Lys	Asn	Cys	Pro	Phe	Asp	Tyr	Ala
	130						135						140		
Cys	Ile	Thr	Asp	Met	Val	Lys	Ser	Ser	Glu	Thr	Thr	Ser	Gly	Asn	Ile
145					150					155				160	
Ala	Phe	Ile	Val	Glu	Leu	Leu	Lys	Asn	Ile	Ser	Thr	Asp	Leu	Ser	Asp
			165						170					175	
Asn	Val	Thr	Arg	Glu	Lys	Met	Lys	Ser	Tyr	Ser	Glu	Val	Ala	Asn	His
	180							185						190	
Ile	Leu	Asp	Thr	Ala	Ala	Ile	Ser	Asn	Trp	Ala	Phe	Ile	Pro	Asn	Lys
	195						200						205		
Asn	Ala	Ser	Ser	Asp	Leu	Leu	Gln	Ser	Val	Asn	Leu	Phe	Ala	Arg	Gln
	210						215						220		
Leu	His	Ile	His	Asn	Asn	Ser	Glu	Asn	Ile	Val	Asn	Glu	Leu	Phe	Ile
225				230					235					240	
Gln	Thr	Lys	Gly	Phe	His	Ile	Asn	His	Asn	Thr	Ser	Glu	Lys	Ser	Leu
			245						250					255	
Asn	Phe	Ser	Met	Ser	Met	Asn	Asn	Thr	Thr	Glu	Asp	Ile	Leu	Gly	Met
	260							265					270		
Val	Gln	Ile	Pro	Arg	Gln	Glu	Leu	Arg	Lys	Leu	Trp	Pro	Asn	Ala	Ser
	275							280					285		
Gln	Ala	Ile	Ser	Ile	Ala	Phe	Pro	Thr	Leu	Gly	Ala	Ile	Leu	Arg	Glu
	290						295						300		
Ala	His	Leu	Gln	Asn	Val	Ser	Leu	Pro	Arg	Gln	Val	Asn	Gly	Leu	Val
305					310					315				320	

122/518

Leu Ser Val Val Leu Pro Glu Arg Leu Gln Glu Ile Ile Leu Thr Phe  
 325 330 335  
 Glu Lys Ile Asn Lys Thr Arg Asn Ala Arg Ala Gln Cys Val Gly Trp  
 340 345 350  
 His Ser Lys Lys Arg Arg Trp Asp Glu Lys Ala Cys Gln Met Met Leu  
 355 360 365  
 Asp Ile Arg Asn Glu Val Lys Cys Arg Cys Asn Tyr Thr Ser Val Val  
 370 375 380  
 Met Ser Phe Ser Ile Leu Met Ser Ser Lys Ser Met Thr Asp Lys Val  
 385 390 395 400  
 Leu Asp Tyr Ile Thr Cys Ile Gly Leu Ser Val Ser Ile Leu Ser Leu  
 405 410 415  
 Val Leu Cys Leu Ile Ile Glu Ala Thr Val Trp Ser Arg Val Val Val  
 420 425 430  
 Thr Glu Ile Ser Tyr Met Arg His Val Cys Ile Val Asn Ile Ala Val  
 435 440 445  
 Ser Leu Leu Thr Ala Asn Val Trp Phe Ile Ile Gly Ser His Phe Asn  
 450 455 460  
 Ile Lys Ala Gln Asp Tyr Asn Met Cys Val Ala Val Thr Phe Phe Ser  
 465 470 475 480  
 His Phe Phe Tyr Leu Ser Leu Phe Phe Trp Met Leu Phe Lys Ala Leu  
 485 490 495  
 Leu Ile Ile Tyr Gly Ile Leu Val Ile Phe Arg Arg Met Met Lys Ser  
 500 505 510  
 Arg Met Met Val Ile Gly Phe Ala Ile Gly Tyr Gly Cys Pro Leu Ile  
 515 520 525  
 Ile Ala Val Thr Thr Val Ala Ile Thr Glu Pro Glu Asn Gly Tyr Met  
 530 535 540  
 Arg Pro Glu Ala Cys Trp Leu Asn Trp Asp Asn Thr Lys Ala Leu Leu

123/518

545	550	555	560
Ala Phe Ala Ile Pro Ala Phe Val Ile Val Ala Val Asn Leu Ile Val			
	565	570	575
Val Leu Val Val Ala Val Asn Thr Gln Arg Pro Ser Ile Gly Ser Ser			
	580	585	590
Lys Ser Gln Asp Val Val Ile Ile Met Arg Ile Ser Lys Asn Val Ala			
	595	600	605
Ile Leu Thr Pro Leu Leu Gly Leu Thr Trp Gly Phe Gly Ile Ala Thr			
	610	615	620
Leu Ile Glu Gly Thr Ser Leu Thr Phe His Ile Ile Phe Ala Leu Leu			
	625	630	635
Asn Ala Phe Gln Val Ser Ser Lys Arg Glu Thr Phe Leu Cys Tyr Ser			
	645	650	655
Asp Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu			
	660	665	670
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly			
	675	680	685
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile			
	690	695	700
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr			
	705	710	715
Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys			
	725	730	735
Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu			
	740	745	750
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu			
	755	760	765
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly			
	770	775	780



124/518

Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr  
 785                      790                      795                      800  
 Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn  
                     805                      810                      815  
 Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser  
                     820                      825                      830  
 Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly  
                     835                      840                      845  
 Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu  
                     850                      855                      860  
 Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe  
 865                      870                      875                      880  
 Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
                     885                      890                      895

&lt;210&gt; 59

&lt;211&gt; 1148

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 59

Met Lys Val Gly Val Leu Trp Leu Ile Ser Phe Phe Thr Phe Thr Asp  
                     5                      10                      15  
 Gly His Gly Gly Phe Leu Gly Lys Asn Asp Gly Ile Lys Thr Lys Lys  
                     20                      25                      30  
 Glu Leu Ile Val Asn Lys Lys Lys His Leu Gly Pro Val Glu Glu Tyr  
                     35                      40                      45  
 Gln Leu Leu Leu Gln Val Thr Tyr Arg Asp Ser Lys Glu Lys Arg Asp  
                     50                      55                      60

125/518

Leu	Arg	Asn	Phe	Leu	Lys	Leu	Leu	Lys	Pro	Pro	Leu	Leu	Trp	Ser	His
65					70					75					80
Gly	Leu	Ile	Arg	Ile	Ile	Arg	Ala	Lys	Ala	Thr	Thr	Asp	Cys	Asn	Ser
				85					90					95	
Leu	Asn	Gly	Val	Leu	Gln	Cys	Thr	Cys	Glu	Asp	Ser	Tyr	Thr	Trp	Phe
				100					105					110	
Pro	Pro	Ser	Cys	Leu	Asp	Pro	Gln	Asn	Cys	Tyr	Leu	His	Thr	Ala	Gly
				115				120						125	
Ala	Leu	Pro	Ser	Cys	Glu	Cys	His	Leu	Asn	Asn	Leu	Ser	Gln	Ser	Val
				130				135						140	
Asn	Phe	Cys	Glu	Arg	Thr	Lys	Ile	Trp	Gly	Thr	Phe	Lys	Ile	Asn	Glu
145						150					155				160
Arg	Phe	Thr	Asn	Asp	Leu	Leu	Asn	Ser	Ser	Ser	Ala	Ile	Tyr	Ser	Lys
				165					170						175
Tyr	Ala	Asn	Gly	Ile	Glu	Ile	Gln	Leu	Lys	Lys	Ala	Tyr	Glu	Arg	Ile
				180					185					190	
Gln	Gly	Phe	Glu	Ser	Val	Gln	Val	Thr	Gln	Phe	Arg	Asn	Gly	Ser	Ile
				195					200					205	
Val	Ala	Gly	Tyr	Glu	Val	Val	Gly	Ser	Ser	Ser	Ala	Ser	Glu	Leu	Leu
				210					215					220	
Ser	Ala	Ile	Glu	His	Val	Ala	Glu	Lys	Ala	Lys	Thr	Ala	Leu	His	Lys
225						230					235				240
Leu	Phe	Pro	Leu	Glu	Asp	Gly	Ser	Phe	Arg	Val	Phe	Gly	Lys	Ala	Gln
				245					250						255
Cys	Asn	Asp	Ile	Val	Phe	Gly	Phe	Gly	Ser	Lys	Asp	Asp	Glu	Tyr	Thr
				260					265					270	
Leu	Pro	Cys	Ser	Ser	Gly	Tyr	Arg	Gly	Asn	Ile	Thr	Ala	Lys	Cys	Glu
				275					280					285	
Ser	Ser	Gly	Trp	Gln	Val	Ile	Arg	Glu	Thr	Cys	Val	Leu	Ser	Leu	Leu

126/518

290	295	300	
Glu Glu Leu Asn Lys Asn Phe Ser Met Ile Val Gly Asn Ala Thr Glu			
305	310	315	320
Ala Ala Val Ser Ser Phe Val Gln Asn Leu Ser Val Ile Ile Arg Gln			
325	330	335	
Asn Pro Ser Thr Thr Val Gly Asn Leu Ala Ser Val Val Ser Ile Leu			
340	345	350	
Ser Asn Ile Ser Ser Leu Ser Leu Ala Ser His Phe Arg Val Ser Asn			
355	360	365	
Ser Thr Met Glu Asp Val Ile Ser Ile Ala Asp Asn Ile Leu Asn Ser			
370	375	380	
Ala Ser Val Thr Asn Trp Thr Val Leu Leu Arg Glu Glu Lys Tyr Ala			
385	390	395	400
Ser Ser Arg Leu Leu Glu Thr Leu Glu Asn Ile Ser Thr Leu Val Pro			
405	410	415	
Pro Thr Ala Leu Pro Leu Asn Phe Ser Arg Lys Phe Ile Asp Trp Lys			
420	425	430	
Gly Ile Pro Val Asn Lys Ser Gln Leu Lys Arg Gly Tyr Ser Tyr Gln			
435	440	445	
Ile Lys Met Cys Pro Gln Asn Thr Ser Ile Pro Ile Arg Gly Arg Val			
450	455	460	
Leu Ile Gly Ser Asp Gln Phe Gln Arg Ser Leu Pro Glu Thr Ile Ile			
465	470	475	480
Ser Met Ala Ser Leu Thr Leu Gly Asn Ile Leu Pro Val Ser Lys Asn			
485	490	495	
Gly Asn Ala Gln Val Asn Gly Pro Val Ile Ser Thr Val Ile Gln Asn			
500	505	510	
Tyr Ser Ile Asn Glu Val Phe Leu Phe Phe Ser Lys Ile Glu Ser Asn			
515	520	525	

127/518

Leu Ser Gln Pro His Cys Val Phe Trp Asp Phe Ser His Leu Gln Trp  
 530 535 540  
 Asn Asp Ala Gly Cys His Leu Val Asn Glu Thr Gln Asp Ile Val Thr  
 545 550 555 560  
 Cys Gln Cys Thr His Leu Thr Ser Phe Ser Ile Leu Met Ser Pro Phe  
 565 570 575  
 Val Pro Ser Thr Ile Phe Pro Val Val Lys Trp Ile Thr Tyr Val Gly  
 580 585 590  
 Leu Gly Ile Ser Ile Gly Ser Leu Ile Leu Cys Leu Ile Ile Glu Ala  
 595 600 605  
 Leu Phe Trp Lys Gln Ile Lys Lys Ser Gln Thr Ser His Thr Arg Arg  
 610 615 620  
 Ile Cys Met Val Asn Ile Ala Leu Ser Leu Leu Ile Ala Asp Val Trp  
 625 630 635 640  
 Phe Ile Val Gly Ala Thr Val Asp Thr Thr Val Asn Pro Ser Gly Val  
 645 650 655  
 Cys Thr Ala Ala Val Phe Phe Thr His Phe Phe Tyr Leu Ser Leu Phe  
 660 665 670  
 Phe Trp Met Leu Met Leu Gly Ile Leu Leu Ala Tyr Arg Ile Ile Leu  
 675 680 685  
 Val Phe His His Met Ala Gln His Leu Met Met Ala Val Gly Phe Cys  
 690 695 700  
 Leu Gly Tyr Gly Cys Pro Leu Ile Ile Ser Val Ile Thr Ile Ala Val  
 705 710 715 720  
 Thr Gln Pro Ser Asn Thr Tyr Lys Arg Lys Asp Val Cys Trp Leu Asn  
 725 730 735  
 Trp Ser Asn Gly Ser Lys Pro Leu Leu Ala Phe Val Val Pro Ala Leu  
 740 745 750  
 Ala Ile Val Ala Val Asn Phe Val Val Val Leu Leu Val Leu Thr Lys

128/518

755	760	765
Leu Trp Arg Pro Thr Val Gly Glu Arg Leu Ser Arg Asp Asp Lys Ala		
770	775	780
Thr Ile Ile Arg Val Gly Lys Ser Leu Leu Ile Leu Thr Pro Leu Leu		
785	790	795
Gly Leu Thr Trp Gly Phe Gly Ile Gly Thr Ile Val Asp Ser Gln Asn		
805	810	815
Leu Ala Trp His Val Ile Phe Ala Leu Leu Asn Ala Phe Gln Gly Phe		
820	825	830
Phe Ile Leu Cys Phe Gly Ile Leu Leu Asp Ser Lys Leu Arg Gln Leu		
835	840	845
Leu Phe Asn Lys Leu Ser Ala Leu Ser Ser Trp Lys Gln Thr Glu Lys		
850	855	860
Gln Asn Ser Ser Asp Leu Ser Ala Lys Pro Lys Phe Ser Lys Pro Phe		
865	870	875
Asn Pro Leu Gln Asn Lys Gly His Tyr Ala Phe Ser His Thr Gly Asp		
885	890	895
Ser Ser Asp Asn Ile Met Leu Thr Gln Phe Val Ser Asn Glu Ala Ser		
900	905	910
Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu		
915	920	925
Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu		
930	935	940
Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr		
945	950	955
Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr		
965	970	975
Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp		
980	985	990

129/518

Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile  
           995                    1000                    1005  
 Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe  
       1010                    1015                    1020  
 Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe  
   1025                    1030                    1035                    1040  
 Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn  
                     1045                    1050                    1055  
 Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys  
                     1060                    1065                    1070  
 Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu  
           1075                    1080                    1085  
 Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu  
       1090                    1095                    1100  
 Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp  
   1105                    1110                    1115                    1120  
 Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala  
                     1125                    1130                    1135  
 Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
                     1140                    1145

&lt;210&gt; 60

&lt;211&gt; 642

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 60

Met Ser Val Lys Pro Ser Trp Gly Pro Gly Pro Ser Glu Gly Val Thr  
                     5                    10                    15

130/518

Ala Val Pro Thr Ser Asp Leu Gly Glu Ile His Asn Trp Thr Glu Leu  
                   20                  25                  30  
 Leu Asp Leu Phe Asn His Thr Leu Ser Glu Cys His Val Glu Leu Ser  
                   35                  40                  45  
 Gln Ser Thr Lys Arg Val Val Leu Phe Ala Leu Tyr Leu Ala Met Phe  
                   50                  55                  60  
 Val Val Gly Leu Val Glu Asn Leu Leu Val Ile Cys Val Asn Trp Arg  
                   65                  70                  75                  80  
 Gly Ser Gly Arg Ala Gly Leu Met Asn Leu Tyr Ile Leu Asn Met Ala  
                   85                  90                  95  
 Ile Ala Asp Leu Gly Ile Val Leu Ser Leu Pro Val Trp Met Leu Glu  
                   100                  105                  110  
 Val Thr Leu Asp Tyr Thr Trp Leu Trp Gly Ser Phe Ser Cys Arg Phe  
                   115                  120                  125  
 Thr His Tyr Phe Tyr Phe Val Asn Met Tyr Ser Ser Ile Phe Phe Leu  
                   130                  135                  140  
 Val Cys Leu Ser Val Asp Arg Tyr Ala Thr Leu Thr Ser Ala Ser Pro  
                   145                  150                  155                  160  
 Ser Trp Gln Arg Tyr Gln His Arg Val Arg Arg Ala Met Cys Ala Gly  
                   165                  170                  175  
 Ile Trp Val Leu Ser Ala Ile Ile Pro Leu Pro Glu Val Val His Ile  
                   180                  185                  190  
 Gln Leu Val Glu Gly Pro Glu Pro Met Cys Leu Phe Met Ala Pro Phe  
                   195                  200                  205  
 Glu Thr Tyr Ser Thr Trp Ala Leu Ala Val Ala Leu Ser Thr Thr Ile  
                   210                  215                  220  
 Leu Gly Phe Leu Leu Pro Phe Pro Leu Ile Thr Val Phe Asn Val Leu  
                   225                  230                  235                  240  
 Thr Ala Cys Arg Leu Arg Gln Pro Gly Gln Pro Lys Ser Arg Arg His

131/518

245	250	255
Cys Leu Leu Leu Cys Ala Tyr Val	Ala Val Phe Val Met Cys Trp Leu	
260	265	270
Pro Tyr His Val Thr Leu Leu Leu Thr	Leu His Gly Thr His Ile	
275	280	285
Ser Leu His Cys His Leu Val His Leu Leu Tyr	Phe Phe Tyr Asp Val	
290	295	300
Ile Asp Cys Phe Ser Met Leu His Cys Val	Ile Asn Pro Ile Leu Tyr	
305	310	315
Asn Phe Leu Ser Pro His Phe Arg Gly Arg	Leu Leu Asn Ala Val Val	
325	330	335
His Tyr Leu Pro Lys Asp Gln Thr Lys Ala Gly	Thr Cys Ala Ser Ser	
340	345	350
Ser Ser Cys Ser Thr Gln His Ser Ile Ile Ile	Thr Lys Gly Asp Ser	
355	360	365
Gln Pro Ala Ala Ala Ala Pro His Pro Glu	Pro Ser Leu Ser Phe Gln	
370	375	380
Ala His His Leu Leu Pro Asn Thr Ser Pro Ile	Ser Pro Thr Gln Pro	
385	390	395
Leu Thr Pro Ser Ala Ser Lys Gly Glu Glu	Leu Phe Thr Gly Val Val	
405	410	415
Pro Ile Leu Val Glu Leu Asp Gly Asp Val	Asn Gly His Lys Phe Ser	
420	425	430
Val Ser Gly Glu Gly Glu Gly Asp Ala Thr	Tyr Gly Lys Leu Thr Leu	
435	440	445
Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro	Val Pro Trp Pro Thr Leu	
450	455	460
Val Thr Thr Leu Cys Tyr Gly Val Gln Cys	Phe Ser Arg Tyr Pro Asp	
465	470	475
		480



132/518

His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr

485

490

495

Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr

500

505

510

Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu

515

520

525

Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys

530

535

540

Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys

545

550

555

560

Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu

565

570

575

Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile

580

585

590

Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln

595

600

605

Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu

610

615

620

Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu

625

630

635

640

Tyr Asn

&lt;210&gt; 61

&lt;211&gt; 653

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 61

Met Val Phe Ala His Arg Met Asp Asn Ser Lys Pro His Leu Ile Ile

133/518

	5		10		15										
Pro	Thr	Leu	Leu	Val	Pro	Leu	Gln	Asn	Arg	Ser	Cys	Thr	Glu	Thr	Ala
	20					25							30		
Thr	Pro	Leu	Pro	Ser	Gln	Tyr	Leu	Met	Glu	Leu	Ser	Glu	Glu	His	Ser
	35					40						45			
Trp	Met	Ser	Asn	Gln	Thr	Asp	Leu	His	Tyr	Val	Leu	Lys	Pro	Gly	Glu
	50					55						60			
Val	Ala	Thr	Ala	Ser	Ile	Phe	Phe	Gly	Ile	Leu	Trp	Leu	Phe	Ser	Ile
	65				70					75				80	
Phe	Gly	Asn	Ser	Leu	Val	Cys	Leu	Val	Ile	His	Arg	Ser	Arg	Arg	Thr
			85						90					95	
Gln	Ser	Thr	Thr	Asn	Tyr	Phe	Val	Val	Ser	Met	Ala	Cys	Ala	Asp	Leu
	100							105						110	
Leu	Ile	Ser	Val	Ala	Ser	Thr	Pro	Phe	Val	Leu	Leu	Gln	Phe	Thr	Thr
	115						120						125		
Gly	Arg	Trp	Thr	Leu	Gly	Ser	Ala	Thr	Cys	Lys	Val	Val	Arg	Tyr	Phe
	130					135							140		
Gln	Tyr	Leu	Thr	Pro	Gly	Val	Gln	Ile	Tyr	Val	Leu	Leu	Ser	Ile	Cys
	145					150				155				160	
Ile	Asp	Arg	Phe	Tyr	Thr	Ile	Val	Tyr	Pro	Leu	Ser	Phe	Lys	Val	Ser
			165					170						175	
Arg	Glu	Lys	Ala	Lys	Lys	Met	Ile	Ala	Ala	Ser	Trp	Ile	Phe	Asp	Ala
		180						185						190	
Gly	Phe	Val	Thr	Pro	Val	Leu	Phe	Phe	Tyr	Gly	Ser	Asn	Trp	Asp	Ser
	195						200						205		
His	Cys	Asn	Tyr	Phe	Leu	Pro	Ser	Ser	Trp	Glu	Gly	Thr	Ala	Tyr	Thr
	210						215						220		
Val	Ile	His	Phe	Leu	Val	Gly	Phe	Val	Ile	Pro	Ser	Val	Leu	Ile	Ile
	225					230				235				240	

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Leu Phe Tyr Gln Lys Val Ile Lys Tyr Ile Trp Arg Ile Gly Thr Asp  
                   245                  250                  255  
 Gly Arg Thr Val Arg Arg Thr Met Asn Ile Val Pro Arg Thr Lys Val  
                   260                  265                  270  
 Lys Thr Ile Lys Met Phe Leu Ile Leu Asn Leu Leu Phe Leu Leu Ser  
                   275                  280                  285  
 Trp Leu Pro Phe His Val Ala Gln Leu Trp His Pro His Glu Gln Asp  
                   290                  295                  300  
 Tyr Lys Lys Ser Ser Leu Val Phe Thr Ala Ile Thr Trp Ile Ser Phe  
 305                  310                  315                  320  
 Ser Ser Ser Ala Ser Lys Pro Thr Leu Tyr Ser Ile Tyr Asn Ala Asn  
                   325                  330                  335  
 Phe Arg Arg Gly Met Lys Glu Thr Phe Cys Met Ser Ser Met Lys Cys  
                   340                  345                  350  
 Tyr Arg Ser Asn Ala Tyr Thr Ile Thr Thr Ser Ser Arg Met Ala Lys  
                   355                  360                  365  
 Lys Asn Tyr Val Gly Ile Ser Glu Ile Pro Ser Met Ala Lys Thr Ile  
                   370                  375                  380  
 Thr Lys Asp Ser Ile Tyr Asp Ser Phe Asp Arg Glu Ala Lys Glu Lys  
 385                  390                  395                  400  
 Lys Leu Ala Trp Pro Ile Asn Ser Asn Pro Pro Asn Thr Phe Val Ala  
                   405                  410                  415  
 Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu  
                   420                  425                  430  
 Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly  
                   435                  440                  445  
 Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr  
                   450                  455                  460  
 Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys

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465                      470                      475                      480  
 Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His  
                          485                      490                      495  
 Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr  
                          500                      505                      510  
 Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys  
                          515                      520                      525  
 Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp  
                          530                      535                      540  
 Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr  
 545                      550                      555                      560  
 Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile  
                          565                      570                      575  
 Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln  
                          580                      585                      590  
 Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val  
                          595                      600                      605  
 Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys  
                          610                      615                      620  
 Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr  
 625                      630                      635                      640  
 Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
                          645                      650

&lt;210&gt; 62

&lt;211&gt; 610

&lt;212&gt; PRT

&lt;213&gt; Human

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&lt;400&gt; 62

Met Ala Cys Asn Ser Thr Ser Leu Glu Ala Tyr Thr Tyr Leu Leu Leu  
                     5                    10                    15  
 Asn Thr Ser Asn Ala Ser Asp Ser Gly Ser Thr Gln Leu Pro Ala Pro  
                     20                    25                    30  
 Leu Arg Ile Ser Leu Ala Ile Val Met Leu Leu Met Thr Val Val Gly  
                     35                    40                    45  
 Phe Leu Gly Asn Thr Val Val Cys Ile Ile Val Tyr Gln Arg Pro Ala  
                     50                    55                    60  
 Met Arg Ser Ala Ile Asn Leu Leu Leu Ala Thr Leu Ala Phe Ser Asp  
                     65                    70                    75                    80  
 Ile Met Leu Ser Leu Cys Cys Met Pro Phe Thr Ala Val Thr Leu Ile  
                     85                    90                    95  
 Thr Val Arg Trp His Phe Gly Asp His Phe Cys Arg Leu Ser Ala Thr  
                     100                    105                    110  
 Leu Tyr Trp Phe Phe Val Leu Glu Gly Val Ala Ile Leu Leu Ile Ile  
                     115                    120                    125  
 Ser Val Asp Arg Phe Leu Ile Ile Val Gln Arg Gln Asp Lys Leu Asn  
                     130                    135                    140  
 Pro Arg Arg Ala Lys Val Ile Ile Ala Val Ser Trp Val Leu Ser Phe  
                     145                    150                    155                    160  
 Cys Ile Ala Gly Pro Ser Leu Thr Gly Trp Thr Leu Val Glu Val Pro  
                     165                    170                    175  
 Ala Arg Ala Pro Gln Cys Val Leu Gly Tyr Thr Glu Leu Pro Ala Asp  
                     180                    185                    190  
 Arg Ala Tyr Val Val Thr Leu Val Val Ala Val Phe Phe Ala Pro Phe  
                     195                    200                    205  
 Gly Val Met Leu Cys Ala Tyr Met Cys Ile Leu Asn Thr Val Arg Lys  
                     210                    215                    220

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Asn Ala Val Arg Val His Asn Gln Ser Asp Ser Leu Asp Leu Arg Gln  
 225                      230                      235                      240  
 Leu Thr Arg Ala Gly Leu Arg Arg Leu Gln Arg Gln Gln Gln Val Ser  
                          245                      250                      255  
 Val Asp Leu Ser Phe Lys Thr Lys Ala Phe Thr Thr Ile Leu Ile Leu  
                          260                      265                      270  
 Phe Val Gly Phe Ser Leu Cys Trp Leu Pro His Ser Val Tyr Ser Leu  
                          275                      280                      285  
 Leu Ser Val Phe Ser Gln Arg Phe Tyr Cys Gly Ser Ser Phe Tyr Ala  
                          290                      295                      300  
 Thr Ser Thr Cys Val Leu Trp Leu Ser Tyr Leu Lys Ser Val Phe Asn  
 305                      310                      315                      320  
 Pro Ile Val Tyr Cys Trp Arg Ile Lys Lys Phe Arg Glu Ala Cys Ile  
                          325                      330                      335  
 Glu Leu Leu Pro Gln Thr Phe Gln Ile Leu Pro Lys Val Pro Glu Arg  
                          340                      345                      350  
 Ile Arg Arg Arg Ile Gln Pro Ser Thr Val Tyr Val Cys Asn Glu Asn  
                          355                      360                      365  
 Gln Ser Ala Val Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val  
                          370                      375                      380  
 Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser  
 385                      390                      395                      400  
 Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu  
                          405                      410                      415  
 Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu  
                          420                      425                      430  
 Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp  
                          435                      440                      445  
 His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr

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450                      455                      460  
 Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr  
 465                      470                      475                      480  
 Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu  
                          485                      490                      495  
 Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys  
                          500                      505                      510  
 Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys  
                          515                      520                      525  
 Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu  
                          530                      535                      540  
 Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile  
 545                      550                      555                      560  
 Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln  
                          565                      570                      575  
 Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu  
                          580                      585                      590  
 Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu  
                          595                      600                      605  
 Tyr Asn  
                          610

&lt;210&gt; 63

&lt;211&gt; 583

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 63

Met Tyr Lys Asp Cys Ile Glu Ser Thr Gly Asp Tyr Phe Leu Leu Cys

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	5	10	15
Asp	Ala	Glu	Gly
Pro	Trp	Gly	Ile
Ile	Ile	Leu	Glu
Ser	Leu	Ala	Ile
Leu			
20	25	30	
Gly	Ile	Val	Val
Thr	Ile	Leu	Leu
Leu	Leu	Leu	Ala
Phe	Leu	Phe	Leu
Met			
35	40	45	
Arg	Lys	Ile	Gln
Asp	Cys	Ser	Gln
Trp	Asn	Val	Leu
Pro	Thr	Gln	Leu
50	55	60	
Leu	Phe	Leu	Leu
Ser	Val	Leu	Gly
Leu	Phe	Gly	Leu
Ala	Phe	Ala	Phe
65	70	75	80
Ile	Ile	Glu	Leu
Asn	Gln	Gln	Thr
Ala	Pro	Val	Arg
Tyr	Phe	Leu	Phe
85	90	95	
Gly	Val	Leu	Phe
Ala	Leu	Cys	Phe
Ser	Cys	Leu	Leu
Ala	His	Ala	Ser
100	105	110	
Asn	Leu	Val	Lys
Leu	Val	Arg	Gly
Cys	Val	Ser	Phe
Ser	Trp	Thr	Thr
115	120	125	
Ile	Leu	Cys	Ile
Ala	Ile	Gly	Cys
Ser	Leu	Leu	Gln
Ile	Ile	Ile	Ala
130	135	140	
Thr	Glu	Tyr	Val
Thr	Leu	Ile	Met
Thr	Arg	Gly	Met
Met	Met	Phe	Val
Asn	145	150	155
Met	Thr	Pro	Cys
Gln	Leu	Asn	Val
Asp	Phe	Val	Val
Leu	Leu	Val	Tyr
165	170	175	
Val	Leu	Phe	Leu
Met	Ala	Leu	Thr
Phe	Phe	Val	Ser
Lys	Ala	Thr	Phe
180	185	190	
Cys	Gly	Pro	Cys
Glu	Asn	Trp	Lys
Gln	His	Gly	Arg
Leu	Ile	Phe	Ile
195	200	205	
Thr	Val	Leu	Phe
Ser	Ile	Ile	Ile
Trp	Val	Val	Trp
Ile	Ser	Met	Leu
210	215	220	
Leu	Arg	Gly	Asn
Pro	Gln	Phe	Gln
Arg	Gln	Pro	Gln
Trp	Asp	Asp	Pro
225	230	235	240



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Val Val Cys Ile Ala Leu Val Thr Asn Ala Trp Val Phe Leu Leu Leu  
 245 250 255  
 Tyr Ile Val Pro Glu Leu Cys Ile Leu Tyr Arg Ser Cys Arg Gln Glu  
 260 265 270  
 Cys Pro Leu Gln Gly Asn Ala Cys Pro Val Thr Ala Tyr Gln His Ser  
 275 280 285  
 Phe Gln Val Glu Asn Gln Glu Leu Ser Arg Ala Arg Asp Ser Asp Gly  
 290 295 300  
 Ala Glu Glu Asp Val Ala Leu Thr Ser Tyr Gly Thr Pro Ile Gln Pro  
 305 310 315 320  
 Gln Thr Val Asp Pro Thr Gln Glu Cys Phe Ile Pro Gln Ala Lys Leu  
 325 330 335  
 Ser Pro Gln Gln Asp Ala Gly Gly Val Ala Ser Lys Gly Glu Glu Leu  
 340 345 350  
 Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn  
 355 360 365  
 Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr  
 370 375 380  
 Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val  
 385 390 395 400  
 Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe  
 405 410 415  
 Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala  
 420 425 430  
 Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp  
 435 440 445  
 Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu  
 450 455 460  
 Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn

141/518

465                      470                      475                      480  
 Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr  
                          485                      490                      495  
 Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr  
                          500                      505                      510  
 Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln  
                          515                      520                      525  
 Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His  
                          530                      535                      540  
 Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg  
 545                      550                      555                      560  
 Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His  
                          565                      570                      575  
 Gly Met Asp Glu Leu Tyr Asn  
                          580

&lt;210&gt; 64

&lt;211&gt; 1205

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 64

Met Pro Ser Pro Pro Gly Leu Arg Ala Leu Trp Leu Cys Ala Ala Leu  
                          5                      10                      15  
 Cys Ala Ser Arg Arg Ala Gly Gly Ala Pro Gln Pro Gly Pro Gly Pro  
                          20                      25                      30  
 Thr Ala Cys Pro Ala Pro Cys His Cys Gln Glu Asp Gly Ile Met Leu  
                          35                      40                      45  
 Ser Ala Asp Cys Ser Glu Leu Gly Leu Ser Ala Val Pro Gly Asp Leu

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50	55	60
Asp Pro Leu Thr Ala Tyr Leu Asp Leu Ser Met Asn Asn Leu Thr Glu		
65	70	75
Leu Gln Pro Gly Leu Phe His His Leu Arg Phe Leu Glu Glu Leu Arg		
85	90	95
Leu Ser Gly Asn His Leu Ser His Ile Pro Gly Gln Ala Phe Ser Gly		
100	105	110
Leu Tyr Ser Leu Lys Ile Leu Met Leu Gln Asn Asn Gln Leu Gly Gly		
115	120	125
Ile Pro Ala Glu Ala Leu Trp Glu Leu Pro Ser Leu Gln Ser Leu Arg		
130	135	140
Leu Asp Ala Asn Leu Ile Ser Leu Val Pro Glu Arg Ser Phe Glu Gly		
145	150	155
Leu Ser Ser Leu Arg His Leu Trp Leu Asp Asp Asn Ala Leu Thr Glu		
165	170	175
Ile Pro Val Arg Ala Leu Asn Asn Leu Pro Ala Leu Gln Ala Met Thr		
180	185	190
Leu Ala Leu Asn Arg Ile Ser His Ile Pro Asp Tyr Ala Phe Gln Asn		
195	200	205
Leu Thr Ser Leu Val Val Leu His Leu His Asn Asn Arg Ile Gln His		
210	215	220
Leu Gly Thr His Ser Phe Glu Gly Leu His Asn Leu Glu Thr Leu Asp		
225	230	235
Leu Asn Tyr Asn Lys Leu Gln Glu Phe Pro Val Ala Ile Arg Thr Leu		
245	250	255
Gly Arg Leu Gln Glu Leu Gly Phe His Asn Asn Asn Ile Lys Ala Ile		
260	265	270
Pro Glu Lys Ala Phe Met Gly Asn Pro Leu Leu Gln Thr Ile His Phe		
275	280	285

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Tyr Asp Asn Pro Ile Gln Phe Val Gly Arg Ser Ala Phe Gln Tyr Leu  
 290 295 300  
 Pro Lys Leu His Thr Leu Ser Leu Asn Gly Ala Met Asp Ile Gln Glu  
 305 310 315 320  
 Phe Pro Asp Leu Lys Gly Thr Thr Ser Leu Glu Ile Leu Thr Leu Thr  
 325 330 335  
 Arg Ala Gly Ile Arg Leu Leu Pro Ser Gly Met Cys Gln Gln Leu Pro  
 340 345 350  
 Arg Leu Arg Val Leu Glu Leu Ser His Asn Gln Ile Glu Glu Leu Pro  
 355 360 365  
 Ser Leu His Arg Cys Gln Lys Leu Glu Glu Ile Gly Leu Gln His Asn  
 370 375 380  
 Arg Ile Trp Glu Ile Gly Ala Asp Thr Phe Ser Gln Leu Ser Ser Leu  
 385 390 395 400  
 Gln Ala Leu Asp Leu Ser Trp Asn Ala Ile Arg Ser Ile His Pro Glu  
 405 410 415  
 Ala Phe Ser Thr Leu His Ser Leu Val Lys Leu Asp Leu Thr Asp Asn  
 420 425 430  
 Gln Leu Thr Thr Leu Pro Leu Ala Gly Leu Gly Gly Leu Met His Leu  
 435 440 445  
 Lys Leu Lys Gly Asn Leu Ala Leu Ser Gln Ala Phe Ser Lys Asp Ser  
 450 455 460  
 Phe Pro Lys Leu Arg Ile Leu Glu Val Pro Tyr Ala Tyr Gln Cys Cys  
 465 470 475 480  
 Pro Tyr Gly Met Cys Ala Ser Phe Phe Lys Ala Ser Gly Gln Trp Glu  
 485 490 495  
 Ala Glu Asp Leu His Leu Asp Asp Glu Glu Ser Ser Lys Arg Pro Leu  
 500 505 510  
 Gly Leu Leu Ala Arg Gln Ala Glu Asn His Tyr Asp Gln Asp Leu Asp

144/518

515	520	525
Glu Leu Gln Leu Glu Met Glu Asp Ser Lys Pro His Pro Ser Val Gln		
530	535	540
Cys Ser Pro Thr Pro Gly Pro Phe Lys Pro Cys Glu Tyr Leu Phe Glu		
545	550	555
Ser Trp Gly Ile Arg Leu Ala Val Trp Ala Ile Val Leu Leu Ser Val		
565	570	575
Leu Cys Asn Gly Leu Val Leu Leu Thr Val Phe Ala Gly Gly Pro Val		
580	585	590
Pro Leu Pro Pro Val Lys Phe Val Val Gly Ala Ile Ala Gly Ala Asn		
595	600	605
Thr Leu Thr Gly Ile Ser Cys Gly Leu Leu Ala Ser Val Asp Ala Leu		
610	615	620
Thr Phe Gly Gln Phe Ser Glu Tyr Gly Ala Arg Trp Glu Thr Gly Leu		
625	630	635
Gly Cys Arg Ala Thr Gly Phe Leu Ala Val Leu Gly Ser Glu Ala Ser		
645	650	655
Val Leu Leu Leu Thr Leu Ala Ala Val Gln Cys Ser Val Ser Val Ser		
660	665	670
Cys Val Arg Ala Tyr Gly Lys Ser Pro Ser Leu Gly Ser Val Arg Ala		
675	680	685
Gly Val Leu Gly Cys Leu Ala Leu Ala Gly Leu Ala Ala Ala Leu Pro		
690	695	700
Leu Ala Ser Val Gly Glu Tyr Gly Ala Ser Pro Leu Cys Leu Pro Tyr		
705	710	715
Ala Pro Pro Glu Gly Gln Pro Ala Ala Leu Gly Phe Thr Val Ala Leu		
725	730	735
Val Met Met Asn Ser Phe Cys Phe Leu Val Val Ala Gly Ala Tyr Ile		
740	745	750

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Lys Leu Tyr Cys Asp Leu Pro Arg Gly Asp Phe Glu Ala Val Trp Asp  
 755 760 765  
 Cys Ala Met Val Arg His Val Ala Trp Leu Ile Phe Ala Asp Gly Leu  
 770 775 780  
 Leu Tyr Cys Pro Val Ala Phe Leu Ser Phe Ala Ser Met Leu Gly Leu  
 785 790 795 800  
 Phe Pro Val Thr Pro Glu Ala Val Lys Ser Val Leu Leu Val Val Leu  
 805 810 815  
 Pro Leu Pro Ala Cys Leu Asn Pro Leu Leu Tyr Leu Leu Phe Asn Pro  
 820 825 830  
 His Phe Arg Asp Asp Leu Arg Arg Leu Arg Pro Arg Ala Gly Asp Ser  
 835 840 845  
 Gly Pro Leu Ala Tyr Ala Ala Ala Gly Glu Leu Glu Lys Ser Ser Cys  
 850 855 860  
 Asp Ser Thr Gln Ala Leu Val Ala Phe Ser Asp Val Asp Leu Ile Leu  
 865 870 875 880  
 Glu Ala Ser Glu Ala Gly Arg Pro Pro Gly Leu Glu Thr Tyr Gly Phe  
 885 890 895  
 Pro Ser Val Thr Leu Ile Ser Cys Gln Gln Pro Gly Ala Pro Arg Leu  
 900 905 910  
 Glu Gly Ser His Cys Val Glu Pro Glu Gly Asn His Phe Gly Asn Pro  
 915 920 925  
 Gln Pro Ser Met Asp Gly Glu Leu Leu Leu Arg Ala Glu Gly Ser Thr  
 930 935 940  
 Pro Ala Gly Gly Gly Leu Ser Gly Gly Gly Gly Phe Gln Pro Ser Gly  
 945 950 955 960  
 Leu Ala Phe Ala Ser His Val Ala Ser Lys Gly Glu Glu Leu Phe Thr  
 965 970 975  
 Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His

146/518

980	985	990
Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys		
995	1000	1005
Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp		
1010	1015	1020
Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg		
1025	1030	1035
Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro		
1045	1050	1055
Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn		
1060	1065	1070
Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn		
1075	1080	1085
Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu		
1090	1095	1100
Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met		
1105	1110	1115
Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His		
1125	1130	1135
Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn		
1140	1145	1150
Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu		
1155	1160	1165
Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His		
1170	1175	1180
Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met		
1185	1190	1195
Asp Glu Leu Tyr Asn		1200
1205		

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&lt;210&gt; 65

&lt;211&gt; 573

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 65

Met Glu Ser Ser Phe Ser Phe Gly Val Ile Leu Ala Val Leu Ala Ser

5

10

15

Leu Ile Ile Ala Thr Asn Thr Leu Val Ala Val Ala Val Leu Leu Leu

20

25

30

Ile His Lys Asn Asp Gly Val Ser Leu Cys Phe Thr Leu Asn Leu Ala

35

40

45

Val Ala Asp Thr Leu Ile Gly Val Ala Ile Ser Gly Leu Leu Thr Asp

50

55

60

Gln Leu Ser Ser Pro Ser Arg Pro Thr Gln Lys Thr Leu Cys Ser Leu

65

70

75

80

Arg Met Ala Phe Val Thr Ser Ser Ala Ala Ala Ser Val Leu Thr Val

85

90

95

Met Leu Ile Thr Phe Asp Arg Tyr Leu Ala Ile Lys Gln Pro Phe Arg

100

105

110

Tyr Leu Lys Ile Met Ser Gly Phe Val Ala Gly Ala Cys Ile Ala Gly

115

120

125

Leu Trp Leu Val Ser Tyr Leu Ile Gly Phe Leu Pro Leu Gly Ile Pro

130

135

140

Met Phe Gln Gln Thr Ala Tyr Lys Gly Gln Cys Ser Phe Phe Ala Val

145

150

155

160

Phe His Pro His Phe Val Leu Thr Leu Ser Cys Val Gly Phe Phe Pro

165

170

175



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Ala Met Leu Leu Phe Val Phe Phe Tyr Cys Asp Met Leu Lys Ile Ala  
 180 185 190  
 Ser Met His Ser Gln Gln Ile Arg Lys Met Glu His Ala Gly Ala Met  
 195 200 205  
 Ala Gly Gly Tyr Arg Ser Pro Arg Thr Pro Ser Asp Phe Lys Ala Leu  
 210 215 220  
 Arg Thr Val Ser Val Leu Ile Gly Ser Phe Ala Leu Ser Trp Thr Pro  
 225 230 235 240  
 Phe Leu Ile Thr Gly Ile Val Gln Val Ala Cys Gln Glu Cys His Leu  
 245 250 255  
 Tyr Leu Val Leu Glu Arg Tyr Leu Trp Leu Leu Gly Val Gly Asn Ser  
 260 265 270  
 Leu Leu Asn Pro Leu Ile Tyr Ala Tyr Trp Gln Lys Glu Val Arg Leu  
 275 280 285  
 Gln Leu Tyr His Met Ala Leu Gly Val Lys Lys Val Leu Thr Ser Phe  
 290 295 300  
 Leu Leu Phe Leu Ser Ala Arg Asn Cys Gly Pro Glu Arg Pro Arg Glu  
 305 310 315 320  
 Ser Ser Cys His Ile Val Thr Ile Ser Ser Ser Glu Phe Asp Gly Ala  
 325 330 335  
 Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu  
 340 345 350  
 Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly  
 355 360 365  
 Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr  
 370 375 380  
 Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys  
 385 390 395 400  
 Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His

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	405		410		415										
Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu	Arg	Thr
	420		425		430										
Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	Val	Lys
	435		440		445										
Phe	Glu	Gly	Asp	Thr	Leu	Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly	Ile	Asp
	450		455		460										
Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	Asn	Tyr
465			470		475									480	
Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	Gly	Ile
			485		490									495	
Lys.	Val	Asn	Phe	Lys	Thr	Arg	His	Asn	Ile	Glu	Asp	Gly	Ser	Val	Gln
	500		505		510										
Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly	Pro	Val
	515		520		525										
Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu	Ser	Lys
	530		535		540										
Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val	Leu	Leu	Glu	Phe	Val	Thr
545			550		555									560	
Ala	Ala	Gly	Ile	Thr	His	Gly	Met	Asp	Glu	Leu	Tyr	Asn			
			565		570										

&lt;210&gt; 66

&lt;211&gt; 612

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 66

Met Leu Thr Gly Ser Cys Gly Asp Pro Gln Lys Lys Pro Gln Val Thr

150/518

	5	10	15
Gln Asp Ser Gly Pro Gln Ser Met Gly Leu Glu Gly Arg Glu Thr Ala			
	20	25	30
Gly Gln Pro Arg Val Thr Leu Leu Pro Thr Pro Asn Val Ser Gly Leu			
	35	40	45
Ser Gln Glu Phe Glu Ser His Trp Pro Glu Ile Ala Glu Arg Ser Pro			
	50	55	60
Cys Val Ala Gly Val Ile Pro Val Ile Tyr Tyr Ser Val Leu Leu Gly			
	65	70	75
Leu Gly Leu Pro Val Ser Leu Leu Thr Ala Val Ala Leu Ala Arg Leu			
	85	90	95
Ala Thr Arg Thr Arg Arg Pro Ser Tyr Tyr Tyr Leu Leu Ala Leu Thr			
	100	105	110
Ala Ser Asp Ile Ile Ile Gln Val Val Ile Val Phe Ala Gly Phe Leu			
	115	120	125
Leu Gln Gly Ala Val Leu Ala Arg Gln Val Pro Gln Ala Val Val Arg			
	130	135	140
Thr Ala Asn Ile Leu Glu Phe Ala Ala Asn His Ala Ser Val Trp Ile			
	145	150	155
Ala Ile Leu Leu Thr Val Asp Arg Tyr Thr Ala Leu Cys His Pro Leu			
	165	170	175
His His Arg Ala Ala Ser Ser Pro Gly Arg Thr Arg Arg Ala Ile Ala			
	180	185	190
Ala Val Leu Ser Ala Ala Leu Leu Thr Gly Ile Pro Phe Tyr Trp Trp			
	195	200	205
Leu Asp Met Trp Arg Asp Thr Asp Ser Pro Arg Thr Leu Asp Glu Val			
	210	215	220
Leu Lys Trp Ala His Cys Leu Thr Val Tyr Phe Ile Pro Cys Gly Val			
	225	230	235
			240

151/518

Phe Leu Val Thr Asn Ser Ala Ile Ile His Arg Leu Arg Arg Arg Gly  
                             245                            250                            255  
 Arg Ser Gly Leu Gln Pro Arg Val Gly Lys Ser Thr Ala Ile Leu Leu  
                             260                            265                            270  
 Gly Ile Thr Thr Leu Phe Thr Leu Leu Trp Ala Pro Arg Val Phe Val  
                             275                            280                            285  
 Met Leu Tyr His Met Tyr Val Ala Pro Val His Arg Asp Trp Arg Val  
                             290                            295                            300  
 His Leu Ala Leu Asp Val Ala Asn Met Val Ala Met Leu His Thr Ala  
 305                            310                            315                            320  
 Ala Asn Phe Gly Leu Tyr Cys Phe Val Ser Lys Thr Phe Arg Ala Thr  
                             325                            330                            335  
 Val Arg Gln Val Ile His Asp Ala Tyr Leu Pro Cys Thr Leu Ala Ser  
                             340                            345                            350  
 Gln Pro Glu Gly Met Ala Ala Lys Pro Val Met Glu Pro Pro Gly Leu  
                             355                            360                            365  
 Pro Thr Gly Ala Glu Val Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly  
                             370                            375                            380  
 Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys  
 385                            390                            395                            400  
 Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu  
                             405                            410                            415  
 Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro  
                             420                            425                            430  
 Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr  
                             435                            440                            445  
 Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu  
                             450                            455                            460  
 Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr

152/518

465                      470                      475                      480  
 Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg  
                          485                      490                      495  
 Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly  
                          500                      505                      510  
 His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala  
                          515                      520                      525  
 Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn  
                          530                      535                      540  
 Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr  
 545                      550                      555                      560  
 Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser  
                          565                      570                      575  
 Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met  
                          580                      585                      590  
 Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp  
                          595                      600                      605  
 Glu Leu Tyr Asn  
                          610

&lt;210&gt; 67

&lt;211&gt; 611

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 67

Met Asp Thr Leu Glu Glu Val Thr Trp Ala Asn Gly Ser Thr Ala Leu  
                          5                      10                      15  
 Pro Pro Pro Leu Ala Pro Asn Ile Ser Val Pro His Arg Cys Leu Leu

				20					25					30				
Leu	Leu	Tyr	Glu	Asp	Ile	Gly	Thr	Ser	Arg	Val	Arg	Tyr	Trp	Asp	Leu			
		35						40					45					
Leu	Leu	Leu	Ile	Pro	Asn	Val	Leu	Phe	Leu	Ile	Phe	Leu	Leu	Trp	Lys			
		50					55					60						
Leu	Pro	Ser	Ala	Arg	Ala	Lys	Ile	Arg	Ile	Thr	Ser	Ser	Pro	Ile	Phe			
65					70					75					80			
Ile	Thr	Phe	Tyr	Ile	Leu	Val	Phe	Val	Val	Ala	Leu	Val	Gly	Ile	Ala			
				85					90						95			
Arg	Ala	Val	Val	Ser	Met	Thr	Val	Ser	Thr	Ser	Asn	Ala	Ala	Thr	Val			
		100						105					110					
Ala	Asp	Lys	Ile	Leu	Trp	Glu	Ile	Thr	Arg	Phe	Phe	Leu	Leu	Ala	Ile			
		115					120					125						
Glu	Leu	Ser	Val	Ile	Ile	Leu	Gly	Leu	Ala	Phe	Gly	His	Leu	Glu	Ser			
	130					135					140							
Lys	Ser	Ser	Ile	Lys	Arg	Val	Leu	Ala	Ile	Thr	Thr	Val	Leu	Ser	Leu			
145				150					155						160			
Ala	Tyr	Ser	Val	Thr	Gln	Gly	Thr	Leu	Glu	Ile	Leu	Tyr	Pro	Asp	Ala			
				165				170						175				
His	Leu	Ser	Ala	Glu	Asp	Phe	Asn	Ile	Tyr	Gly	His	Gly	Gly	Arg	Gln			
		180					185						190					
Phe	Trp	Leu	Val	Ser	Ser	Cys	Phe	Phe	Phe	Leu	Val	Tyr	Ser	Leu	Val			
	195					200						205						
Val	Ile	Leu	Pro	Lys	Thr	Pro	Leu	Lys	Glu	Arg	Ile	Ser	Leu	Pro	Ser			
	210					215						220						
Arg	Arg	Ser	Phe	Tyr	Val	Tyr	Ala	Gly	Ile	Leu	Ala	Leu	Leu	Asn	Leu			
225				230					235					240				
Leu	Gln	Gly	Leu	Gly	Ser	Val	Leu	Leu	Cys	Phe	Asp	Ile	Ile	Glu	Gly			
				245					250					255				

154/518

Leu Cys Cys Val Asp Ala Thr Thr Phe Leu Tyr Phe Ser Phe Phe Ala  
 260 265 270  
 Pro Leu Ile Tyr Val Ala Phe Leu Arg Gly Phe Phe Gly Ser Glu Pro  
 275 280 285  
 Lys Ile Leu Phe Ser Tyr Lys Cys Gln Val Asp Glu Thr Glu Glu Pro  
 290 295 300  
 Asp Val His Leu Pro Gln Pro Tyr Ala Val Ala Arg Arg Glu Gly Leu  
 305 310 315 320  
 Glu Ala Ala Gly Ala Ala Gly Ala Ser Ala Ala Ser Tyr Ser Ser Thr  
 325 330 335  
 Gln Phe Asp Ser Ala Gly Gly Val Ala Tyr Leu Asp Asp Ile Ala Ser  
 340 345 350  
 Met Pro Cys His Thr Gly Ser Ile Asn Ser Thr Asp Ser Glu Arg Trp  
 355 360 365  
 Lys Ala Ile Asn Ala Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val  
 370 375 380  
 Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe  
 385 390 395 400  
 Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr  
 405 410 415  
 Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr  
 420 425 430  
 Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro  
 435 440 445  
 Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly  
 450 455 460  
 Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys  
 465 470 475 480  
 Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile

155/518

	485		490		495										
Glu	Leu	Lys	Gly	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn	Ile	Leu	Gly	His
	500		505		510										
Lys	Leu	Glu	Tyr	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr	Ile	Met	Ala	Asp
	515		520		525										
Lys	Gln	Lys	Asn	Gly	Ile	Lys	Val	Asn	Phe	Lys	Thr	Arg	His	Asn	Ile
	530		535		540										
Glu	Asp	Gly	Ser	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln	Gln	Asn	Thr	Pro
545			550		555									560	
Ile	Gly	Asp	Gly	Pro	Val	Leu	Leu	Pro	Asp	Asn	His	Tyr	Leu	Ser	Thr
			565		570									575	
Gln	Ser	Ala	Leu	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg	Asp	His	Met	Val
			580		585									590	
Leu	Leu	Glu	Phe	Val	Thr	Ala	Ala	Gly	Ile	Thr	His	Gly	Met	Asp	Glu
			595		600									605	
Leu	Tyr	Asn													
	610														

&lt;210&gt; 68

&lt;211&gt; 671

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 68

Met	Cys	Phe	Ser	Pro	Ile	Leu	Glu	Ile	Asn	Met	Gln	Ser	Glu	Ser	Asn
			5						10					15	
Ile	Thr	Val	Arg	Asp	Asp	Ile	Asp	Asp	Ile	Asn	Thr	Asn	Met	Tyr	Gln
			20						25					30	
Pro	Leu	Ser	Tyr	Pro	Leu	Ser	Phe	Gln	Val	Ser	Leu	Thr	Gly	Phe	Leu



156/518

35	40	45
Met Leu Glu Ile Val Leu Gly Leu Gly Ser Asn Leu Thr Val Leu Val		
50	55	60
Leu Tyr Cys Met Lys Ser Asn Leu Ile Asn Ser Val Ser Asn Ile Ile		
65	70	75
Thr Met Asn Leu His Val Leu Asp Val Ile Ile Cys Val Gly Cys Ile		
85	90	95
Pro Leu Thr Ile Val Ile Leu Leu Leu Ser Leu Glu Ser Asn Thr Ala		
100	105	110
Leu Ile Cys Cys Phe His Glu Ala Cys Val Ser Phe Ala Ser Val Ser		
115	120	125
Thr Ala Ile Asn Val Phe Ala Ile Thr Leu Asp Arg Tyr Asp Ile Ser		
130	135	140
Val Lys Pro Ala Asn Arg Ile Leu Thr Met Gly Arg Ala Val Met Leu		
145	150	155
Met Ile Ser Ile Trp Ile Phe Ser Phe Phe Ser Phe Leu Ile Pro Phe		
165	170	175
Ile Glu Val Asn Phe Phe Ser Leu Gln Ser Gly Asn Thr Trp Glu Asn		
180	185	190
Lys Thr Leu Leu Cys Val Ser Thr Asn Glu Tyr Tyr Thr Glu Leu Gly		
195	200	205
Met Tyr Tyr His Leu Leu Val Gln Ile Pro Ile Phe Phe Phe Thr Val		
210	215	220
Val Val Met Leu Ile Thr Tyr Thr Lys Ile Leu Gln Ala Leu Asn Ile		
225	230	235
Arg Ile Gly Thr Arg Phe Ser Thr Gly Gln Lys Lys Lys Ala Arg Lys		
245	250	255
Lys Lys Thr Ile Ser Leu Thr Thr Gln His Glu Ala Thr Asp Met Ser		
260	265	270

157/518

Gln Ser Ser Gly Gly Arg Asn Val Val Phe Gly Val Arg Thr Ser Val  
 275 280 285  
 Ser Val Ile Ile Ala Leu Arg Arg Ala Val Lys Arg His Arg Glu Arg  
 290 295 300  
 Arg Glu Arg Gln Lys Arg Val Phe Arg Met Ser Leu Leu Ile Ile Ser  
 305 310 315 320  
 Thr Phe Leu Leu Cys Trp Thr Pro Ile Ser Val Leu Asn Thr Thr Ile  
 325 330 335  
 Leu Cys Leu Gly Pro Ser Asp Leu Leu Val Lys Leu Arg Leu Cys Phe  
 340 345 350  
 Leu Val Met Ala Tyr Gly Thr Thr Ile Phe His Pro Leu Leu Tyr Ala  
 355 360 365  
 Phe Thr Arg Gln Lys Phe Gln Lys Val Leu Lys Ser Lys Met Lys Lys  
 370 375 380  
 Arg Val Val Ser Ile Val Glu Ala Asp Pro Leu Pro Asn Asn Ala Val  
 385 390 395 400  
 Ile His Asn Ser Trp Ile Asp Pro Lys Arg Asn Lys Lys Ile Thr Phe  
 405 410 415  
 Glu Asp Ser Glu Ile Arg Glu Lys Cys Leu Val Pro Gln Val Val Thr  
 420 425 430  
 Asp Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu  
 435 440 445  
 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly  
 450 455 460  
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile  
 465 470 475 480  
 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr  
 485 490 495  
 Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys

158/518

500	505	510
Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu		
515	520	525
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu		
530	535	540
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly		
545	550	555
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr		
565	570	575
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn		
580	585	590
Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser		
595	600	605
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly		
610	615	620
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu		
625	630	635
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe		
645	650	655
Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn		
660	665	670

&lt;210&gt; 69

&lt;211&gt; 599

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 69

Met Asn Glu Ser Arg Trp Thr Glu Trp Arg Ile Leu Asn Met Ser Ser

				5					10					15					
Gly	Ile	Val	Asn	Val	Ser	Glu	Arg	His	Ser	Cys	Pro	Leu	Gly	Phe	Gly				
			20						25					30					
His	Tyr	Ser	Val	Val	Asp	Val	Cys	Ile	Phe	Glu	Thr	Val	Val	Ile	Val				
		35						40					45						
Leu	Leu	Thr	Phe	Leu	Ile	Ile	Ala	Gly	Asn	Leu	Thr	Val	Ile	Phe	Val				
		50					55					60							
Phe	His	Cys	Ala	Pro	Leu	Leu	His	His	Tyr	Thr	Thr	Ser	Tyr	Phe	Ile				
	65					70				75					80				
Gln	Thr	Met	Ala	Tyr	Ala	Asp	Leu	Phe	Val	Gly	Val	Ser	Cys	Leu	Val				
				85					90					95					
Pro	Thr	Leu	Ser	Leu	Leu	His	Tyr	Ser	Thr	Gly	Val	His	Glu	Ser	Leu				
			100					105					110						
Thr	Cys	Gln	Val	Phe	Gly	Tyr	Ile	Ile	Ser	Val	Leu	Lys	Ser	Val	Ser				
		115					120					125							
Met	Ala	Cys	Leu	Ala	Cys	Ile	Ser	Val	Asp	Arg	Tyr	Leu	Ala	Ile	Thr				
	130					135					140								
Lys	Pro	Leu	Ser	Tyr	Asn	Gln	Leu	Val	Thr	Pro	Cys	Arg	Leu	Arg	Ile				
	145				150					155					160				
Cys	Ile	Ile	Leu	Ile	Trp	Ile	Tyr	Ser	Cys	Leu	Ile	Phe	Leu	Pro	Ser				
			165						170				175						
Phe	Phe	Gly	Trp	Gly	Lys	Pro	Gly	Tyr	His	Gly	Asp	Ile	Phe	Glu	Trp				
		180						185					190						
Cys	Ala	Thr	Ser	Trp	Leu	Thr	Ser	Ala	Tyr	Phe	Thr	Gly	Phe	Ile	Val				
		195					200					205							
Cys	Leu	Leu	Tyr	Ala	Pro	Ala	Ala	Phe	Val	Val	Cys	Phe	Thr	Tyr	Phe				
	210					215					220								
His	Ile	Phe	Lys	Ile	Cys	Arg	Gln	His	Thr	Lys	Glu	Ile	Asn	Asp	Arg				
225					230					235					240				

160/518

Arg Ala Arg Phe Pro Ser His Glu Val Asp Ser Ser Arg Glu Thr Gly  
 245 250 255  
 His Ser Pro Asp Arg Arg Tyr Ala Met Val Leu Phe Arg Ile Thr Ser  
 260 265 270  
 Val Phe Tyr Met Leu Trp Leu Pro Tyr Ile Ile Tyr Phe Leu Leu Glu  
 275 280 285  
 Ser Ser Arg Val Leu Asp Asn Pro Thr Leu Ser Phe Leu Thr Thr Trp  
 290 295 300  
 Leu Ala Ile Ser Asn Ser Phe Cys Asn Cys Val Ile Tyr Ser Leu Ser  
 305 310 315 320  
 Asn Ser Val Phe Arg Leu Gly Leu Arg Arg Leu Ser Glu Thr Met Cys  
 325 330 335  
 Thr Ser Cys Met Cys Val Lys Asp Gln Glu Ala Gln Glu Pro Lys Pro  
 340 345 350  
 Arg Lys Arg Ala Asn Ser Cys Ser Ile Ala Ser Lys Gly Glu Glu Leu  
 355 360 365  
 Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn  
 370 375 380  
 Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr  
 385 390 395 400  
 Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val  
 405 410 415  
 Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe  
 420 425 430  
 Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala  
 435 440 445  
 Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp  
 450 455 460  
 Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu

161/518

465                      470                      475                      480  
 Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn  
                          485                      490                      495  
 Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr  
                          500                      505                      510  
 Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr  
                          515                      520                      525  
 Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln  
                          530                      535                      540  
 Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His  
 545                      550                      555                      560  
 Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg  
                          565                      570                      575  
 Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His  
                          580                      585                      590  
 Gly Met Asp Glu Leu Tyr Asn  
                          595

&lt;210&gt; 70

&lt;211&gt; 575

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 70

Met Asn Ser Trp Asp Ala Gly Leu Ala Gly Leu Leu Val Gly Thr Met  
                          5                      10                      15  
 Gly Val Ser Leu Leu Ser Asn Ala Leu Val Leu Leu Cys Leu Leu His  
                          20                      25                      30  
 Ser Ala Asp Ile Arg Arg Gln Ala Pro Ala Leu Phe Thr Leu Asn Leu

162/518

35	40	45
Thr Cys Gly Asn Leu Leu Cys Thr Val Val Asn Met Pro Leu Thr Leu		
50	55	60
Ala Gly Val Val Ala Gln Arg Gln Pro Ala Gly Asp Arg Leu Cys Arg		
65	70	75
Leu Ala Ala Phe Leu Asp Thr Phe Leu Ala Ala Asn Ser Met Leu Ser		
85	90	95
Met Ala Ala Leu Ser Ile Asp Arg Trp Val Ala Val Val Phe Pro Leu		
100	105	110
Ser Tyr Arg Ala Lys Met Arg Leu Arg Asp Ala Ala Leu Met Val Ala		
115	120	125
Tyr Thr Trp Leu His Ala Leu Thr Phe Pro Ala Ala Ala Leu Ala Leu		
130	135	140
Ser Trp Leu Gly Phe His Gln Leu Tyr Ala Ser Cys Thr Leu Cys Ser		
145	150	155
Arg Arg Pro Asp Glu Arg Leu Arg Phe Ala Val Phe Thr Gly Ala Phe		
165	170	175
His Ala Leu Ser Phe Leu Leu Ser Phe Val Val Leu Cys Cys Thr Tyr		
180	185	190
Leu Lys Val Leu Lys Val Ala Arg Phe His Cys Lys Arg Ile Asp Val		
195	200	205
Ile Thr Met Gln Thr Leu Val Leu Leu Val Asp Leu His Pro Ser Val		
210	215	220
Arg Glu Arg Cys Leu Glu Glu Gln Lys Arg Arg Arg Gln Arg Ala Thr		
225	230	235
Lys Lys Ile Ser Thr Phe Ile Gly Thr Phe Leu Val Cys Phe Ala Pro		
245	250	255
Tyr Val Ile Thr Arg Leu Val Glu Leu Phe Ser Thr Val Pro Ile Gly		
260	265	270

163/518

Ser His Trp Gly Val Leu Ser Lys Cys Leu Ala Tyr Ser Lys Ala Ala  
 275 280 285  
 Ser Asp Pro Phe Val Tyr Ser Leu Leu Arg His Gln Tyr Arg Lys Ser  
 290 295 300  
 Cys Lys Glu Ile Leu Asn Arg Leu Leu His Arg Arg Ser Ile His Ser  
 305 310 315 320  
 Ser Gly Leu Thr Gly Asp Ser His Ser Gln Asn Ile Leu Pro Val Ser  
 325 330 335  
 Glu Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu  
 340 345 350  
 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly  
 355 360 365  
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile  
 370 375 380  
 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr  
 385 390 395 400  
 Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys  
 405 410 415  
 Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu  
 420 425 430  
 Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu  
 435 440 445  
 Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly  
 450 455 460  
 Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr  
 465 470 475 480  
 Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn  
 485 490 495  
 Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser



164/518

500	505	510	
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly			
515	520	525	
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu			
530	535	540	
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe			
545	550	555	560
Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn			
565	570	575	

&lt;210&gt; 71

&lt;211&gt; 727

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 71

Met Asn Pro Pro Ser Gly Pro Arg Val Leu Pro Ser Pro Thr Gln Glu			
5	10	15	
Pro Ser Cys Met Ala Thr Pro Ala Pro Pro Ser Trp Trp Asp Ser Ser			
20	25	30	
Gln Ser Ser Ile Ser Ser Leu Gly Arg Leu Pro Ser Ile Ser Pro Thr			
35	40	45	
Ala Pro Gly Thr Trp Ala Ala Ala Trp Val Pro Leu Pro Thr Val Asp			
50	55	60	
Val Pro Asp His Ala His Tyr Thr Leu Gly Thr Val Ile Leu Leu Val			
65	70	75	80
Gly Leu Thr Gly Met Leu Gly Asn Leu Thr Val Ile Tyr Thr Phe Cys			
85	90	95	
Arg Ala Val Leu Arg Gly Val Thr Val Met Met Gln Ser Arg Ser Leu			

165/518

100	105	110
Arg Thr Pro Ala Asn Met Phe Ile Ile Asn Leu Ala Val Ser Asp Phe		
115	120	125
Leu Met Ser Phe Thr Gln Ala Pro Val Phe Phe Thr Ser Ser Leu Tyr		
130	135	140
Lys Gln Trp Leu Phe Gly Glu Thr Gly Cys Glu Phe Tyr Ala Phe Cys		
145	150	155
Gly Ala Leu Phe Gly Ile Ser Ser Met Ile Thr Leu Thr Ala Ile Ala		
165	170	175
Leu Asp Arg Tyr Leu Val Ile Thr Arg Pro Leu Ala Thr Phe Gly Val		
180	185	190
Ala Ser Lys Arg Arg Ala Ala Phe Val Leu Leu Gly Val Trp Leu Tyr		
195	200	205
Ala Leu Ala Trp Ser Leu Pro Pro Phe Phe Gly Trp Ser Ala Tyr Val		
210	215	220
Pro Glu Gly Leu Leu Thr Ser Cys Ser Trp Asp Tyr Met Ser Phe Thr		
225	230	235
Pro Ala Val Arg Ala Tyr Thr Met Leu Leu Cys Cys Phe Val Phe Phe		
245	250	255
Leu Pro Leu Leu Ile Ile Ile Tyr Cys Tyr Ile Phe Ile Phe Arg Ala		
260	265	270
Ile Arg Glu Thr Gly Arg Ala Leu Gln Thr Phe Gly Ala Cys Lys Gly		
275	280	285
Asn Gly Glu Ser Leu Trp Gln Arg Gln Arg Leu Gln Ser Glu Cys Lys		
290	295	300
Met Ala Lys Ile Met Leu Leu Val Ile Leu Leu Phe Val Leu Ser Trp		
305	310	315
Ala Pro Tyr Ser Ala Val Ala Leu Val Ala Phe Ala Gly Tyr Ala His		
325	330	335

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Val Leu Thr Pro Tyr Met Ser Ser Val Pro Ala Val Ile Ala Lys Ala  
 340 345 350  
 Ser Ala Ile His Asn Pro Ile Ile Tyr Ala Ile Thr His Pro Lys Tyr  
 355 360 365  
 Arg Val Ala Ile Ala Gln His Leu Pro Cys Leu Gly Val Leu Leu Gly  
 370 375 380  
 Val Ser Arg Arg His Ser Arg Pro Tyr Pro Ser Tyr Arg Ser Thr His  
 385 390 395 400  
 Arg Ser Thr Leu Ile Ser His Thr Ser Asn Leu Ser Trp Ile Ser Ile  
 405 410 415  
 Arg Arg Arg Gln Glu Ser Leu Gly Ser Glu Ser Glu Val Gly Trp Thr  
 420 425 430  
 His Met Glu Ala Ala Ala Val Trp Gly Ala Ala Gln Gln Ala Asn Gly  
 435 440 445  
 Arg Ser Leu Tyr Gly Gln Gly Leu Glu Asp Leu Glu Ala Lys Ala Pro  
 450 455 460  
 Pro Arg Pro Gln Gly His Glu Ala Glu Thr Pro Gly Lys Thr Lys Gly  
 465 470 475 480  
 Leu Ile Pro Ser Gln Asp Pro Arg Met Ala Ser Lys Gly Glu Glu Leu  
 485 490 495  
 Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn  
 500 505 510  
 Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr  
 515 520 525  
 Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val  
 530 535 540  
 Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe  
 545 550 555 560  
 Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala

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	565		570		575										
Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp
	580		585		590										
Gly	Asn	Tyr	Lys	Thr	Arg	Ala	Glu	Val	Lys	Phe	Glu	Gly	Asp	Thr	Leu
	595		600		605										
Val	Asn	Arg	Ile	Glu	Leu	Lys	Gly	Ile	Asp	Phe	Lys	Glu	Asp	Gly	Asn
	610		615		620										
Ile	Leu	Gly	His	Lys	Leu	Glu	Tyr	Asn	Tyr	Asn	Ser	His	Asn	Val	Tyr
625			630		635									640	
Ile	Met	Ala	Asp	Lys	Gln	Lys	Asn	Gly	Ile	Lys	Val	Asn	Phe	Lys	Thr
	645		650		655										
Arg	His	Asn	Ile	Glu	Asp	Gly	Ser	Val	Gln	Leu	Ala	Asp	His	Tyr	Gln
	660		665		670										
Gln	Asn	Thr	Pro	Ile	Gly	Asp	Gly	Pro	Val	Leu	Leu	Pro	Asp	Asn	His
	675		680		685										
Tyr	Leu	Ser	Thr	Gln	Ser	Ala	Leu	Ser	Lys	Asp	Pro	Asn	Glu	Lys	Arg
	690		695		700										
Asp	His	Met	Val	Leu	Leu	Glu	Phe	Val	Thr	Ala	Ala	Gly	Ile	Thr	His
705			710		715									720	
Gly	Met	Asp	Glu	Leu	Tyr	Asn									
	725														

&lt;210&gt; 72

&lt;211&gt; 616

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 72

Met Val Trp Gly Lys Ile Cys Trp Phe Ser Gln Arg Ala Gly Trp Thr

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	5		10		15
Val Phe Ala Glu Ser Gln Ile Ser Leu Ser Cys Ser Leu Cys Leu His					
	20		25		30
Ser Gly Asp Gln Glu Ala Gln Asn Pro Asn Leu Val Ser Gln Leu Cys					
	35		40		45
Gly Val Phe Leu Gln Asn Glu Thr Asn Glu Thr Ile His Met Gln Met					
	50		55		60
Ser Met Ala Val Gly Gln Gln Ala Leu Pro Leu Asn Ile Ile Ala Pro					
	65		70		75
Lys Ala Val Leu Val Ser Leu Cys Gly Val Leu Leu Asn Gly Thr Val					
	85		90		95
Phe Trp Leu Leu Cys Cys Gly Ala Thr Asn Pro Tyr Met Val Tyr Ile					
	100		105		110
Leu His Leu Val Ala Ala Asp Val Ile Tyr Leu Cys Cys Ser Ala Val					
	115		120		125
Gly Phe Leu Gln Val Thr Leu Leu Thr Tyr His Gly Val Val Phe Phe					
	130		135		140
Ile Pro Asp Phe Leu Ala Ile Leu Ser Pro Phe Ser Phe Glu Val Cys					
	145		150		155
Leu Cys Leu Leu Val Ala Ile Ser Thr Glu Arg Cys Val Cys Val Leu					
	165		170		175
Phe Pro Ile Trp Tyr Arg Cys His Arg Pro Lys Tyr Thr Ser Asn Val					
	180		185		190
Val Cys Thr Leu Ile Trp Gly Leu Pro Phe Cys Ile Asn Ile Val Lys					
	195		200		205
Ser Leu Phe Leu Thr Tyr Trp Lys His Val Lys Ala Cys Val Ile Phe					
	210		215		220
Leu Lys Leu Ser Gly Leu Phe His Ala Ile Leu Ser Leu Val Met Cys					
	225		230		235
					240

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Val	Ser	Ser	Leu	Thr	Leu	Leu	Ile	Arg	Phe	Leu	Cys	Cys	Ser	Gln	Gln
			245						250					255	
Gln	Lys	Ala	Thr	Arg	Val	Tyr	Ala	Val	Val	Gln	Ile	Ser	Ala	Pro	Met
			260					265						270	
Phe	Leu	Leu	Trp	Ala	Leu	Pro	Leu	Ser	Val	Ala	Pro	Leu	Ile	Thr	Asp
			275					280						285	
Phe	Lys	Met	Phe	Val	Thr	Thr	Ser	Tyr	Leu	Ile	Ser	Leu	Phe	Leu	Ile
		290					295				300				
Ile	Asn	Ser	Ser	Ala	Asn	Pro	Ile	Ile	Tyr	Phe	Phe	Val	Gly	Ser	Leu
305					310					315				320	
Arg	Lys	Lys	Arg	Leu	Lys	Glu	Ser	Leu	Arg	Val	Ile	Leu	Gln	Arg	Ala
			325						330					335	
Leu	Ala	Asp	Lys	Pro	Glu	Val	Gly	Arg	Asn	Lys	Lys	Ala	Ala	Gly	Ile
			340					345						350	
Asp	Pro	Met	Glu	Gln	Pro	His	Ser	Thr	Gln	His	Val	Glu	Asn	Leu	Leu
		355						360					365		
Pro	Arg	Glu	His	Arg	Val	Asp	Val	Glu	Thr	Ala	Ser	Lys	Gly	Glu	Glu
		370					375					380			
Leu	Phe	Thr	Gly	Val	Val	Pro	Ile	Leu	Val	Glu	Leu	Asp	Gly	Asp	Val
385				390						395				400	
Asn	Gly	His	Lys	Phe	Ser	Val	Ser	Gly	Glu	Gly	Glu	Gly	Asp	Ala	Thr
			405						410				415		
Tyr	Gly	Lys	Leu	Thr	Leu	Lys	Phe	Ile	Cys	Thr	Thr	Gly	Lys	Leu	Pro
			420					425					430		
Val	Pro	Trp	Pro	Thr	Leu	Val	Thr	Thr	Leu	Cys	Tyr	Gly	Val	Gln	Cys
			435					440					445		
Phe	Ser	Arg	Tyr	Pro	Asp	His	Met	Lys	Arg	His	Asp	Phe	Phe	Lys	Ser
		450					455				460				
Ala	Met	Pro	Glu	Gly	Tyr	Val	Gln	Glu	Arg	Thr	Ile	Phe	Phe	Lys	Asp

170/518

465                      470                      475                      480  
 Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr  
                          485                      490                      495  
 Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly  
                          500                      505                      510  
 Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val  
                          515                      520                      525  
 Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys  
                          530                      535                      540  
 Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr  
 545                      550                      555                      560  
 Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn  
                          565                      570                      575  
 His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys  
                          580                      585                      590  
 Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr  
                          595                      600                      605  
 His Gly Met Asp Glu Leu Tyr Asn  
                          610                      615

&lt;210&gt; 73

&lt;211&gt; 608

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 73

Met Ala Asn Tyr Ser His Ala Ala Asp Asn Ile Leu Gln Asn Leu Ser  
                          5                      10                      15  
 Pro Leu Thr Ala Phe Leu Lys Leu Thr Ser Leu Gly Phe Ile Ile Gly

171/518

	20	25	30
Val Ser Val Val Gly Asn Leu Leu Ile Ser Ile Leu Leu Val Lys Asp			
35	40	45	
Lys Thr Leu His Arg Ala Pro Tyr Tyr Phe Leu Leu Asp Leu Cys Cys			
50	55	60	
Ser Asp Ile Leu Arg Ser Ala Ile Cys Phe Pro Phe Val Phe Asn Ser			
65	70	75	80
Val Lys Asn Gly Ser Thr Trp Thr Tyr Gly Thr Leu Thr Cys Lys Val			
85	90	95	
Ile Ala Phe Leu Gly Val Leu Ser Cys Phe His Thr Ala Phe Met Leu			
100	105	110	
Phe Cys Ile Ser Val Thr Arg Tyr Leu Ala Ile Ala His His Arg Phe			
115	120	125	
Tyr Thr Lys Arg Leu Thr Phe Trp Thr Cys Leu Ala Val Ile Cys Met			
130	135	140	
Val Trp Thr Leu Ser Val Ala Met Ala Phe Pro Pro Val Leu Asp Val			
145	150	155	160
Gly Thr Tyr Ser Phe Ile Arg Glu Glu Asp Gln Cys Thr Phe Gln His			
165	170	175	
Arg Ser Phe Arg Ala Asn Asp Ser Leu Gly Phe Met Leu Leu Leu Ala			
180	185	190	
Leu Ile Leu Leu Ala Thr Gln Leu Val Tyr Leu Lys Leu Ile Phe Phe			
195	200	205	
Val His Asp Arg Arg Lys Met Lys Pro Val Gln Phe Val Ala Ala Val			
210	215	220	
Ser Gln Asn Trp Thr Phe His Gly Pro Gly Ala Ser Gly Gln Ala Ala			
225	230	235	240
Ala Asn Trp Leu Ala Gly Phe Gly Arg Gly Pro Thr Pro Pro Thr Leu			
245	250	255	



172/518

Leu Gly Ile Arg Gln Asn Ala Asn Thr Thr Gly Arg Arg Arg Leu Leu  
 260 265 270  
 Val Leu Asp Glu Phe Lys Met Glu Lys Arg Ile Ser Arg Met Phe Tyr  
 275 280 285  
 Ile Met Thr Phe Leu Phe Leu Thr Leu Trp Gly Pro Tyr Leu Val Ala  
 290 295 300  
 Cys Tyr Trp Arg Val Phe Ala Arg Gly Pro Val Val Pro Gly Gly Phe  
 305 310 315 320  
 Leu Thr Ala Ala Val Trp Met Ser Phe Ala Gln Ala Gly Ile Asn Pro  
 325 330 335  
 Phe Val Cys Ile Phe Ser Asn Arg Glu Leu Arg Arg Cys Phe Ser Thr  
 340 345 350  
 Thr Leu Leu Tyr Cys Arg Lys Ser Arg Leu Pro Arg Glu Pro Tyr Cys  
 355 360 365  
 Val Ile Ser Arg Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile  
 370 375 380  
 Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser  
 385 390 395 400  
 Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe  
 405 410 415  
 Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr  
 420 425 430  
 Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met  
 435 440 445  
 Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln  
 450 455 460  
 Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala  
 465 470 475 480  
 Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys

173/518

	485	490	495
Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu			
500	505	510	
Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys			
515	520	525	
Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly			
530	535	540	
Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp			
545	550	555	560
Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala			
565	570	575	
Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu			
580	585	590	
Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn			
595	600	605	

&lt;210&gt; 74

&lt;211&gt; 572

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 74

Met Asn Glu Asp Leu Lys Val Asn Leu Ser Gly Leu Pro Arg Asp Tyr			
5	10	15	
Leu Asp Ala Ala Ala Ala Glu Asn Ile Ser Ala Ala Val Ser Ser Arg			
20	25	30	
Val Pro Ala Val Glu Pro Glu Pro Glu Leu Val Val Asn Pro Trp Asp			
35	40	45	
Ile Val Leu Cys Thr Ser Gly Thr Leu Ile Ser Cys Glu Asn Ala Ile			

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50	55	60
Val Val Leu Ile Ile Phe His Asn Pro Ser Leu Arg Ala Pro Met Phe		
65	70	75
Leu Leu Ile Gly Ser Leu Ala Leu Ala Asp Leu Leu Ala Gly Ile Gly		
85	90	95
Leu Ile Thr Asn Phe Val Phe Ala Tyr Leu Leu Gln Ser Glu Ala Thr		
100	105	110
Lys Leu Val Thr Ile Gly Leu Ile Val Ala Ser Phe Ser Ala Ser Val		
115	120	125
Cys Ser Leu Leu Ala Ile Thr Val Asp Arg Tyr Leu Ser Leu Tyr Tyr		
130	135	140
Ala Leu Thr Tyr His Ser Glu Arg Thr Val Thr Phe Thr Tyr Val Met		
145	150	155
Leu Val Met Leu Trp Gly Thr Ser Ile Cys Leu Gly Leu Leu Pro Val		
165	170	175
Met Gly Trp Asn Cys Leu Arg Asp Glu Ser Thr Cys Ser Val Val Arg		
180	185	190
Pro Leu Thr Lys Asn Asn Ala Ala Ile Leu Ser Val Ser Phe Leu Phe		
195	200	205
Met Phe Ala Leu Met Leu Gln Leu Tyr Ile Gln Ile Cys Lys Ile Val		
210	215	220
Met Arg His Ala His Gln Ile Ala Leu Gln His His Phe Leu Ala Thr		
225	230	235
Ser His Tyr Val Thr Thr Arg Lys Gly Val Ser Thr Leu Ala Ile Ile		
245	250	255
Leu Gly Thr Phe Ala Ala Cys Trp Met Pro Phe Thr Leu Tyr Ser Leu		
260	265	270
Ile Ala Asp Tyr Thr Tyr Pro Ser Ile Tyr Thr Tyr Ala Thr Leu Leu		
275	280	285

175/518

Pro Ala Thr Tyr Asn Ser Ile Ile Asn Pro Val Ile Tyr Ala Phe Arg  
 290 295 300  
 Asn Gln Glu Ile Gln Lys Ala Leu Cys Leu Ile Cys Cys Gly Cys Ile  
 305 310 315 320  
 Pro Ser Ser Leu Ala Gln Arg Ala Arg Ser Pro Ser Asp Val Ala Ser  
 325 330 335  
 Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu  
 340 345 350  
 Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu  
 355 360 365  
 Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr  
 370 375 380  
 Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr  
 385 390 395 400  
 Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp  
 405 410 415  
 Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile  
 420 425 430  
 Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe  
 435 440 445  
 Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe  
 450 455 460  
 Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn  
 465 470 475 480  
 Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys  
 485 490 495  
 Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu  
 500 505 510  
 Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu

176/518

515                      520                      525  
 Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp  
 530                      535                      540  
 Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala  
 545                      550                      555                      560  
 Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
                          565                      570

&lt;210&gt; 75

&lt;211&gt; 613

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 75

Met Asp Val Thr Ser Gln Ala Arg Gly Val Gly Leu Glu Met Tyr Leu  
                          5                      10                      15  
 Gly Thr Ala Gln Pro Ala Ala Pro Asn Thr Thr Ser Pro Glu Leu Asn  
                          20                      25                      30  
 Leu Ser His Pro Leu Leu Gly Thr Ala Leu Ala Asn Gly Thr Gly Glu  
                          35                      40                      45  
 Leu Ser Glu His Gln Gln Tyr Val Ile Gly Leu Phe Leu Ser Cys Leu  
                          50                      55                      60  
 Tyr Thr Ile Phe Leu Phe Pro Ile Gly Phe Val Gly Asn Ile Leu Ile  
                          65                      70                      75                      80  
 Leu Val Val Asn Ile Ser Phe Arg Glu Lys Met Thr Ile Pro Asp Leu  
                          85                      90                      95  
 Tyr Phe Ile Asn Leu Ala Val Ala Asp Leu Ile Leu Val Ala Asp Ser  
                          100                      105                      110  
 Leu Ile Glu Val Phe Asn Leu His Glu Arg Tyr Tyr Asp Ile Ala Val

177/518

115	120	125
Leu Cys Thr Phe Met Ser Leu Phe Leu Gln Val Asn Met Tyr Ser Ser		
130	135	140
Val Phe Phe Leu Thr Trp Met Ser Phe Asp Arg Tyr Ile Ala Leu Ala		
145	150	155
Arg Ala Met Arg Cys Ser Leu Phe Arg Thr Lys His His Ala Arg Leu		
165	170	175
Ser Cys Gly Leu Ile Trp Met Ala Ser Val Ser Ala Thr Leu Val Pro		
180	185	190
Phe Thr Ala Val His Leu Gln His Thr Asp Glu Ala Cys Phe Cys Phe		
195	200	205
Ala Asp Val Arg Glu Val Gln Trp Leu Glu Val Thr Leu Gly Phe Ile		
210	215	220
Val Pro Phe Ala Ile Ile Gly Leu Cys Tyr Ser Leu Ile Val Arg Val		
225	230	235
Leu Val Arg Ala His Arg His Arg Gly Leu Arg Pro Arg Arg Gln Lys		
245	250	255
Ala Leu Arg Met Ile Leu Ala Val Val Leu Val Phe Phe Val Cys Trp		
260	265	270
Leu Pro Glu Asn Val Phe Ile Ser Val His Leu Leu Gln Arg Thr Gln		
275	280	285
Pro Gly Ala Ala Pro Cys Lys Gln Ser Phe Arg His Ala His Pro Leu		
290	295	300
Thr Gly His Ile Val Asn Leu Ala Ala Phe Ser Asn Ser Cys Leu Asn		
305	310	315
Pro Leu Ile Tyr Ser Phe Leu Gly Glu Thr Phe Arg Asp Lys Leu Arg		
325	330	335
Leu Tyr Ile Glu Gln Lys Thr Asn Leu Pro Ala Leu Asn Arg Phe Cys		
340	345	350

178/518

His Ala Ala Leu Lys Ala Val Ile Pro Asp Ser Thr Glu Gln Ser Asp  
 355 360 365  
 Val Arg Phe Ser Ser Ala Val Ala Ser Lys Gly Glu Glu Leu Phe Thr  
 370 375 380  
 Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His  
 385 390 395 400  
 Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys  
 405 410 415  
 Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp  
 420 425 430  
 Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg  
 435 440 445  
 Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro  
 450 455 460  
 Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn  
 465 470 475 480  
 Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn  
 485 490 495  
 Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu  
 500 505 510  
 Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met  
 515 520 525  
 Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His  
 530 535 540  
 Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn  
 545 550 555 560  
 Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu  
 565 570 575  
 Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His

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      580                      585                      590
Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met
      595                      600                      605
Asp Glu Leu Tyr Asn
      610

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<210> 76  
 <211> 574  
 <212> PRT  
 <213> Human

<400> 76

Met	Asn	Asn	Asn	Thr	Thr	Cys	Ile	Gln	Pro	Ser	Met	Ile	Ser	Ser	Met
				5					10					15	
Ala	Leu	Pro	Ile	Ile	Tyr	Ile	Leu	Leu	Cys	Ile	Val	Gly	Val	Phe	Gly
				20				25						30	
Asn	Thr	Leu	Ser	Gln	Trp	Ile	Phe	Leu	Thr	Lys	Ile	Gly	Lys	Lys	Thr
			35				40					45			
Ser	Thr	His	Ile	Tyr	Leu	Ser	His	Leu	Val	Thr	Ala	Asn	Leu	Leu	Val
	50					55					60				
Cys	Ser	Ala	Met	Pro	Phe	Met	Ser	Ile	Tyr	Phe	Leu	Lys	Gly	Phe	Gln
65					70					75					80
Trp	Glu	Tyr	Gln	Ser	Ala	Gln	Cys	Arg	Val	Val	Asn	Phe	Leu	Gly	Thr
				85					90					95	
Leu	Ser	Met	His	Ala	Ser	Met	Phe	Val	Ser	Leu	Leu	Ile	Leu	Ser	Trp
				100				105					110		
Ile	Ala	Ile	Ser	Arg	Tyr	Ala	Thr	Leu	Met	Gln	Lys	Asp	Ser	Ser	Gln
				115				120				125			
Glu	Thr	Thr	Ser	Cys	Tyr	Glu	Lys	Ile	Phe	Tyr	Gly	His	Leu	Leu	Lys



180/518

130	135	140	
Lys Phe Arg Gln Pro Asn Phe Ala Arg Lys Leu Cys Ile Tyr Ile Trp			
145	150	155	160
Gly Val Val Leu Gly Ile Ile Ile Pro Val Thr Val Tyr Tyr Ser Val			
165	170	175	
Ile Glu Ala Thr Glu Gly Glu Glu Ser Leu Cys Tyr Asn Arg Gln Met			
180	185	190	
Glu Leu Gly Ala Met Ile Ser Gln Ile Ala Gly Leu Ile Gly Thr Thr			
195	200	205	
Phe Ile Gly Phe Ser Phe Leu Val Val Leu Thr Ser Tyr Tyr Ser Phe			
210	215	220	
Val Ser His Leu Arg Lys Ile Arg Thr Cys Thr Ser Ile Met Glu Lys			
225	230	235	240
Asp Leu Thr Tyr Ser Ser Val Lys Arg His Leu Leu Val Ile Gln Ile			
245	250	255	
Leu Leu Ile Val Cys Phe Leu Pro Tyr Ser Ile Phe Lys Pro Ile Phe			
260	265	270	
Tyr Val Leu His Gln Arg Asp Asn Cys Gln Gln Leu Asn Tyr Leu Ile			
275	280	285	
Glu Thr Lys Asn Ile Leu Thr Cys Leu Ala Ser Ala Arg Ser Ser Thr			
290	295	300	
Asp Pro Ile Ile Phe Leu Leu Leu Asp Lys Thr Phe Lys Lys Thr Leu			
305	310	315	320
Tyr Asn Leu Phe Thr Lys Ser Asn Ser Ala His Met Gln Ser Tyr Gly			
325	330	335	
Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val			
340	345	350	
Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu			
355	360	365	

181/518

Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys  
 370 375 380  
 Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu  
 385 390 395 400  
 Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg  
 405 410 415  
 His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg  
 420 425 430  
 Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val  
 435 440 445  
 Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile  
 450 455 460  
 Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn  
 465 470 475 480  
 Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly  
 485 490 495  
 Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val  
 500 505 510  
 Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro  
 515 520 525  
 Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser  
 530 535 540  
 Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val  
 545 550 555 560  
 Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
 565 570

&lt;210&gt; 77

&lt;211&gt; 1061

182/518

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 77

Met Gly Gly Arg Val Phe Leu Val Phe Leu Ala Phe Cys Val Trp Leu  
                     5                    10                    15  
 Thr Leu Pro Gly Ala Glu Thr Gln Asp Ser Arg Gly Cys Ala Arg Trp  
                     20                    25                    30  
 Cys Pro Gln Asp Ser Ser Cys Val Asn Ala Thr Ala Cys Arg Cys Asn  
                     35                    40                    45  
 Pro Gly Phe Ser Ser Phe Ser Glu Ile Ile Thr Thr Pro Met Glu Thr  
                     50                    55                    60  
 Cys Asp Asp Ile Asn Glu Cys Ala Thr Leu Ser Lys Val Ser Cys Gly  
                     65                    70                    75                    80  
 Lys Phe Ser Asp Cys Trp Asn Thr Glu Gly Ser Tyr Asp Cys Val Cys  
                     85                    90                    95  
 Ser Pro Gly Tyr Glu Pro Val Ser Gly Ala Lys Thr Phe Lys Asn Glu  
                     100                    105                    110  
 Ser Glu Asn Thr Cys Gln Asp Val Asp Glu Cys Gln Gln Asn Pro Arg  
                     115                    120                    125  
 Leu Cys Lys Ser Tyr Gly Thr Cys Val Asn Thr Leu Gly Ser Tyr Thr  
                     130                    135                    140  
 Cys Gln Cys Leu Pro Gly Phe Lys Phe Ile Pro Glu Asp Pro Lys Val  
                     145                    150                    155                    160  
 Cys Thr Asp Val Asn Glu Cys Thr Ser Gly Gln Asn Pro Cys His Ser  
                     165                    170                    175  
 Ser Thr His Cys Leu Asn Asn Val Gly Ser Tyr Gln Cys Arg Cys Arg  
                     180                    185                    190  
 Pro Gly Trp Gln Pro Ile Pro Gly Ser Pro Asn Gly Pro Asn Asn Thr

183/518

195	200	205
Val Cys Glu Asp Val Asp Glu Cys Ser Ser Gly Gln His Gln Cys Asp		
210	215	220
Ser Ser Thr Val Cys Phe Asn Thr Val Gly Ser Tyr Ser Cys Arg Cys		
225	230	235
Arg Pro Gly Trp Lys Pro Arg His Gly Ile Pro Asn Asn Gln Lys Asp		
245	250	255
Thr Val Cys Glu Asp Met Thr Phe Ser Thr Trp Thr Pro Pro Pro Gly		
260	265	270
Val His Ser Gln Thr Leu Ser Arg Phe Phe Asp Lys Val Gln Asp Leu		
275	280	285
Gly Arg Asp Tyr Lys Pro Gly Leu Ala Asn Asn Thr Ile Gln Ser Ile		
290	295	300
Leu Gln Ala Leu Asp Glu Leu Leu Glu Val Pro Gly Asp Leu Glu Thr		
305	310	315
Leu Pro Arg Leu Gln Gln His Cys Val Ala Ser His Leu Leu Asp Gly		
325	330	335
Leu Glu Asp Val Leu Arg Gly Leu Ser Lys Asn Leu Ser Asn Gly Leu		
340	345	350
Leu Asn Phe Ser Tyr Pro Ala Gly Thr Glu Leu Ser Leu Glu Val Gln		
355	360	365
Lys Gln Val Asp Arg Ser Val Thr Leu Arg Gln Asn Gln Ala Val Met		
370	375	380
Gln Leu Asp Trp Asn Gln Ala Gln Lys Ser Gly Asp Pro Gly Pro Ser		
385	390	395
Val Val Gly Leu Val Ser Ile Pro Gly Met Gly Lys Leu Leu Ala Glu		
405	410	415
Ala Pro Leu Val Leu Glu Pro Glu Lys Gln Met Leu Leu His Glu Thr		
420	425	430

184/518

His Gln Gly Leu Leu Gln Asp Gly Ser Pro Ile Leu Leu Ser Asp Val  
 435 440 445  
 Ile Ser Ala Phe Leu Ser Asn Asn Asp Thr Gln Asn Leu Ser Ser Pro  
 450 455 460  
 Val Thr Phe Thr Phe Ser His Arg Ser Val Ile Pro Arg Gln Lys Val  
 465 470 475 480  
 Leu Cys Val Phe Trp Glu His Gly Gln Asn Gly Cys Gly His Trp Ala  
 485 490 495  
 Thr Thr Gly Cys Ser Thr Ile Gly Thr Arg Asp Thr Ser Thr Ile Cys  
 500 505 510  
 Arg Cys Thr His Leu Ser Ser Phe Ala Val Leu Met Ala His Tyr Asp  
 515 520 525  
 Val Gln Glu Glu Asp Pro Val Leu Thr Val Ile Thr Tyr Met Gly Leu  
 530 535 540  
 Ser Val Ser Leu Leu Cys Leu Leu Leu Ala Ala Leu Thr Phe Leu Leu  
 545 550 555 560  
 Cys Lys Ala Ile Gln Asn Thr Ser Thr Ser Leu His Leu Gln Leu Ser  
 565 570 575  
 Leu Cys Leu Phe Leu Ala His Leu Leu Phe Leu Val Ala Ile Asp Gln  
 580 585 590  
 Thr Gly His Lys Val Leu Cys Ser Ile Ile Ala Gly Thr Leu His Tyr  
 595 600 605  
 Leu Tyr Leu Ala Thr Leu Thr Trp Met Leu Leu Glu Ala Leu Tyr Leu  
 610 615 620  
 Phe Leu Thr Ala Arg Asn Leu Thr Val Val Asn Tyr Ser Ser Ile Asn  
 625 630 635 640  
 Arg Phe Met Lys Lys Leu Met Phe Pro Val Gly Tyr Gly Val Pro Ala  
 645 650 655  
 Val Thr Val Ala Ile Ser Ala Ala Ser Arg Pro His Leu Tyr Gly Thr

185/518

660	665	670
Pro Ser Arg Cys Trp Leu Gln	Pro Glu Lys Gly Phe Ile Trp Gly Phe	
675	680	685
Leu Gly Pro Val Cys Ala Ile Phe Ser Val Asn Leu Val Leu Phe Leu		
690	695	700
Val Thr Leu Trp Ile Leu Lys Asn Arg Leu Ser Ser Leu Asn Ser Glu		
705	710	715
Val Ser Thr Leu Arg Asn Thr Arg Met Leu Ala Phe Lys Ala Thr Ala		
725	730	735
Gln Leu Phe Ile Leu Gly Cys Thr Trp Cys Leu Gly Ile Leu Gln Val		
740	745	750
Gly Pro Ala Ala Arg Val Met Ala Tyr Leu Phe Thr Ile Ile Asn Ser		
755	760	765
Leu Gln Gly Val Phe Ile Phe Leu Val Tyr Cys Leu Leu Ser Gln Gln		
770	775	780
Val Arg Glu Gln Tyr Gly Lys Trp Ser Lys Gly Ile Arg Lys Leu Lys		
785	790	795
Thr Glu Ser Glu Met His Thr Leu Ser Ser Ser Ala Lys Ala Asp Thr		
805	810	815
Ser Lys Pro Ser Thr Val Asn Ala Ser Lys Gly Glu Glu Leu Phe Thr		
820	825	830
Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His		
835	840	845
Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys		
850	855	860
Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp		
865	870	875
Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg		
885	890	895

186/518

Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro  
                   900                  905                  910  
 Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn  
                   915                  920                  925  
 Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn  
                   930                  935                  940  
 Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu  
 945                  950                  955                  960  
 Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met  
                   965                  970                  975  
 Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His  
                   980                  985                  990  
 Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn  
                   995                  1000                  1005  
 Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu  
                   1010                  1015                  1020  
 Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His  
 1025                  1030                  1035                  1040  
 Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met  
                   1045                  1050                  1055  
 Asp Glu Leu Tyr Asn  
                   1060

&lt;210&gt; 78

&lt;211&gt; 753

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 78

187/518

Met Gly His Asn Gly Ser Trp Ile Ser Pro Asn Ala Ser Glu Pro His  
                     5                    10                    15  
 Asn Ala Ser Gly Ala Glu Ala Ala Gly Val Asn Arg Ser Ala Leu Gly  
                     20                    25                    30  
 Glu Phe Gly Glu Ala Gln Leu Tyr Arg Gln Phe Thr Thr Thr Val Gln  
                     35                    40                    45  
 Val Val Ile Phe Ile Gly Ser Leu Leu Gly Asn Phe Met Val Leu Trp  
                     50                    55                    60  
 Ser Thr Cys Arg Thr Thr Val Phe Lys Ser Val Thr Asn Arg Phe Ile  
                     65                    70                    75                    80  
 Lys Asn Leu Ala Cys Ser Gly Ile Cys Ala Ser Leu Val Cys Val Pro  
                     85                    90                    95  
 Phe Asp Ile Ile Leu Ser Thr Ser Pro His Cys Cys Trp Trp Ile Tyr  
                     100                    105                    110  
 Thr Met Leu Phe Cys Lys Val Val Lys Phe Leu His Lys Val Phe Cys  
                     115                    120                    125  
 Ser Val Thr Ile Leu Ser Phe Pro Ala Ile Ala Leu Asp Arg Tyr Tyr  
                     130                    135                    140  
 Ser Val Leu Tyr Pro Leu Glu Arg Lys Ile Ser Asp Ala Lys Ser Arg  
                     145                    150                    155                    160  
 Glu Leu Val Met Tyr Ile Trp Ala His Ala Val Val Ala Ser Val Pro  
                     165                    170                    175  
 Val Phe Ala Val Thr Asn Val Ala Asp Ile Tyr Ala Thr Ser Thr Cys  
                     180                    185                    190  
 Thr Glu Val Trp Ser Asn Ser Leu Gly His Leu Val Tyr Val Leu Val  
                     195                    200                    205  
 Tyr Asn Ile Thr Thr Val Ile Val Pro Val Val Val Val Phe Leu Phe  
                     210                    215                    220  
 Leu Ile Leu Ile Arg Arg Ala Leu Ser Ala Ser Gln Lys Lys Lys Val



188/518

225	230	235	240
Ile Ile Ala Ala Leu Arg Thr Pro Gln Asn Thr Ile Ser Ile Pro Tyr			
245	250	255	
Ala Ser Gln Arg Glu Ala Glu Leu His Ala Thr Leu Leu Ser Met Val			
260	265	270	
Met Val Phe Ile Leu Cys Ser Val Pro Tyr Ala Thr Leu Val Val Tyr			
275	280	285	
Gln Thr Val Leu Asn Val Pro Asp Thr Ser Val Phe Leu Leu Leu Thr			
290	295	300	
Ala Val Trp Leu Pro Lys Val Ser Leu Leu Ala Asn Pro Val Leu Phe			
305	310	315	320
Leu Thr Val Asn Lys Ser Val Arg Lys Cys Leu Ile Gly Thr Leu Val			
325	330	335	
Gln Leu His His Arg Tyr Ser Arg Arg Asn Val Val Ser Thr Gly Ser			
340	345	350	
Gly Met Ala Glu Ala Ser Leu Glu Pro Ser Ile Arg Ser Gly Ser Gln			
355	360	365	
Leu Leu Glu Met Phe His Ile Gly Gln Gln Gln Ile Phe Lys Pro Thr			
370	375	380	
Glu Asp Glu Glu Glu Ser Glu Ala Lys Tyr Ile Gly Ser Ala Asp Phe			
385	390	395	400
Gln Ala Lys Glu Ile Phe Ser Thr Cys Leu Glu Gly Glu Gln Gly Pro			
405	410	415	
Gln Phe Ala Pro Ser Ala Pro Pro Leu Ser Thr Val Asp Ser Val Ser			
420	425	430	
Gln Val Ala Pro Ala Ala Pro Val Glu Pro Glu Thr Phe Pro Asp Lys			
435	440	445	
Tyr Ser Leu Gln Phe Gly Phe Gly Pro Phe Glu Leu Pro Pro Gln Trp			
450	455	460	

189/518

Leu Ser Glu Thr Arg Asn Ser Lys Lys Arg Leu Leu Pro Pro Leu Gly  
 465 470 475 480  
 Asn Thr Pro Glu Glu Leu Ile Gln Thr Lys Val Pro Lys Val Gly Arg  
 485 490 495  
 Val Glu Arg Lys Met Ser Arg Asn Asn Lys Val Ser Ile Phe Pro Lys  
 500 505 510  
 Val Asp Ser Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro  
 515 520 525  
 Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val  
 530 535 540  
 Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys  
 545 550 555 560  
 Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val  
 565 570 575  
 Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His  
 580 585 590  
 Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val  
 595 600 605  
 Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg  
 610 615 620  
 Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu  
 625 630 635 640  
 Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu  
 645 650 655  
 Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln  
 660 665 670  
 Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp  
 675 680 685  
 Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly

190/518

690	695	700
Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser		
705	710	715
Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu		
725	730	735
Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr		
740	745	750

Asn

&lt;210&gt; 79

&lt;211&gt; 600

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 79

Met Asp Leu His Leu Phe Asp Tyr Ala Glu Pro Gly Asn Phe Ser Asp		
5	10	15
Ile Ser Trp Pro Cys Asn Ser Ser Asp Cys Ile Val Val Asp Thr Val		
20	25	30
Met Cys Pro Asn Met Pro Asn Lys Ser Val Leu Leu Tyr Thr Leu Ser		
35	40	45
Phe Ile Tyr Ile Phe Ile Phe Val Ile Gly Met Ile Ala Asn Ser Val		
50	55	60
Val Val Trp Val Asn Ile Gln Ala Lys Thr Thr Gly Tyr Asp Thr His		
65	70	75
Cys Tyr Ile Leu Asn Leu Ala Ile Ala Asp Leu Trp Val Val Leu Thr		
85	90	95
Ile Pro Val Trp Val Val Ser Leu Val Gln His Asn Gln Trp Pro Met		
100	105	110

191/518

Gly Glu Leu Thr Cys Lys Val Thr His Leu Ile Phe Ser Ile Asn Leu  
 115 120 125  
 Phe Gly Ser Ile Phe Phe Leu Thr Cys Met Ser Val Asp Arg Tyr Leu  
 130 135 140  
 Ser Ile Thr Tyr Phe Thr Asn Thr Pro Ser Ser Arg Lys Lys Met Val  
 145 150 155 160  
 Arg Arg Val Val Cys Ile Leu Val Trp Leu Leu Ala Phe Cys Val Ser  
 165 170 175  
 Leu Pro Asp Thr Tyr Tyr Leu Lys Thr Val Thr Ser Ala Ser Asn Asn  
 180 185 190  
 Glu Thr Tyr Cys Arg Ser Phe Tyr Pro Glu His Ser Ile Lys Glu Trp  
 195 200 205  
 Leu Ile Gly Met Glu Leu Val Ser Val Val Leu Gly Phe Ala Val Pro  
 210 215 220  
 Phe Ser Ile Ile Ala Val Phe Tyr Phe Leu Leu Ala Arg Ala Ile Ser  
 225 230 235 240  
 Ala Ser Ser Asp Gln Glu Lys His Ser Ser Arg Lys Ile Ile Phe Ser  
 245 250 255  
 Tyr Val Val Val Phe Leu Val Cys Trp Leu Pro Tyr His Val Ala Val  
 260 265 270  
 Leu Leu Asp Ile Phe Ser Ile Leu His Tyr Ile Pro Phe Thr Cys Arg  
 275 280 285  
 Leu Glu His Ala Leu Phe Thr Ala Leu His Val Thr Gln Cys Leu Ser  
 290 295 300  
 Leu Val His Cys Cys Val Asn Pro Val Leu Tyr Ser Phe Ile Asn Arg  
 305 310 315 320  
 Asn Tyr Arg Tyr Glu Leu Met Lys Ala Phe Ile Phe Lys Tyr Ser Ala  
 325 330 335  
 Lys Thr Gly Leu Thr Lys Leu Ile Asp Ala Ser Arg Val Ser Glu Thr

192/518

340	345	350	
Glu Tyr Ser Ala Leu Glu Gln Ser Thr Lys Ala Ser Lys Gly Glu Glu			
355	360	365	
Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val			
370	375	380	
Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr			
385	390	395	400
Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro			
405	410	415	
Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys			
420	425	430	
Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser			
435	440	445	
Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp			
450	455	460	
Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr			
465	470	475	480
Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly			
485	490	495	
Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val			
500	505	510	
Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys			
515	520	525	
Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr			
530	535	540	
Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn			
545	550	555	560
His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys			
565	570	575	

193/518

Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr

580

585

590

His Gly Met Asp Glu Leu Tyr Asn

595

600

&lt;210&gt; 80

&lt;211&gt; 672

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 80

Met Glu Asp Leu Phe Ser Pro Ser Ile Leu Pro Pro Ala Pro Asn Ile

5

10

15

Ser Val Pro Ile Leu Leu Gly Trp Gly Leu Asn Leu Thr Leu Gly Gln

20

25

30

Gly Ala Pro Ala Ser Gly Pro Pro Ser Arg Arg Val Arg Leu Val Phe

35

40

45

Leu Gly Val Ile Leu Val Val Ala Val Ala Gly Asn Thr Thr Val Leu

50

55

60

Cys Arg Leu Cys Gly Gly Gly Gly Pro Trp Ala Gly Pro Lys Arg Arg

65

70

75

80

Lys Met Asp Phe Leu Leu Val Gln Leu Ala Leu Ala Asp Leu Tyr Ala

85

90

95

Cys Gly Gly Thr Ala Leu Ser Gln Leu Ala Trp Glu Leu Leu Gly Glu

100

105

110

Pro Arg Ala Ala Thr Gly Asp Leu Ala Cys Arg Phe Leu Gln Leu Leu

115

120

125

Gln Ala Ser Gly Arg Gly Ala Ser Ala His Leu Val Val Leu Ile Ala

130

135

140

194/518

Leu Glu Arg Arg Arg Ala Val Arg Leu Pro His Gly Arg Pro Leu Pro  
 145                      150                      155                      160  
 Ala Arg Ala Leu Ala Ala Leu Gly Trp Leu Leu Ala Leu Leu Ala  
                          165                      170                      175  
 Leu Pro Pro Ala Phe Val Val Arg Gly Asp Ser Pro Ser Pro Leu Pro  
                          180                      185                      190  
 Pro Pro Pro Pro Pro Thr Ser Leu Gln Pro Gly Ala Pro Pro Ala Ala  
                          195                      200                      205  
 Arg Ala Trp Pro Gly Gln Arg Arg Cys His Gly Ile Phe Ala Pro Leu  
                          210                      215                      220  
 Pro Arg Trp His Leu Gln Val Tyr Ala Phe Tyr Glu Ala Val Ala Gly  
 225                      230                      235                      240  
 Phe Val Ala Pro Val Thr Val Leu Gly Val Ala Cys Gly His Leu Leu  
                          245                      250                      255  
 Ser Val Trp Trp Arg His Arg Pro Gln Ala Pro Ala Ala Ala Ala Pro  
                          260                      265                      270  
 Trp Ser Ala Ser Pro Gly Arg Ala Pro Ala Pro Ser Ala Leu Pro Arg  
                          275                      280                      285  
 Ala Lys Val Gln Ser Leu Lys Met Ser Leu Leu Leu Ala Leu Leu Phe  
                          290                      295                      300  
 Val Gly Cys Glu Leu Pro Tyr Phe Ala Ala Arg Leu Ala Ala Ala Trp  
 305                      310                      315                      320  
 Ser Ser Gly Pro Ala Gly Asp Trp Glu Gly Glu Gly Leu Ser Ala Ala  
                          325                      330                      335  
 Leu Arg Val Val Ala Met Ala Asn Ser Ala Leu Asn Pro Phe Val Tyr  
                          340                      345                      350  
 Leu Phe Phe Gln Ala Gly Asp Cys Arg Leu Arg Arg Gln Leu Arg Lys  
                          355                      360                      365  
 Arg Leu Gly Ser Leu Cys Cys Ala Pro Gln Gly Gly Ala Glu Asp Glu

195/518

370	375	380	
Glu Gly Pro Arg Gly His Gln Ala Leu Tyr Arg Gln Arg Trp Pro His			
385	390	395	400
Pro His Tyr His His Ala Arg Arg Glu Pro Leu Asp Glu Gly Gly Leu			
405	410	415	
Arg Pro Pro Pro Pro Arg Pro Arg Pro Leu Pro Cys Ser Cys Glu Ser			
420	425	430	
Ala Phe Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile			
435	440	445	
Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser			
450	455	460	
Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe			
465	470	475	480
Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr			
485	490	495	
Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met			
500	505	510	
Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln			
515	520	525	
Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala			
530	535	540	
Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys			
545	550	555	560
Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu			
565	570	575	
Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys			
580	585	590	
Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly			
595	600	605	



196/518

Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp  
610 615 620  
Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala  
625 630 635 640  
Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu  
645 650 655  
Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
660 665 670

&lt;210&gt; 81

&lt;211&gt; 542

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 81

Met Leu Ser Thr Gly Val Val Ser Phe Phe Ser Leu Lys Ser Asp Ser  
5 10 15  
Ala Pro Pro Trp Met Val Leu Ala Val Leu Trp Cys Ser Met Ala Gln  
20 25 30  
Thr Leu Leu Leu Pro Ser Phe Ile Trp Ser Cys Glu Arg Tyr Arg Ala  
35 40 45  
Asp Val Arg Thr Val Trp Glu Gln Cys Val Ala Ile Met Ser Glu Glu  
50 55 60  
Asp Gly Asp Asp Asp Gly Gly Cys Asp Asp Tyr Ala Glu Gly Arg Val  
65 70 75 80  
Cys Lys Val Arg Phe Asp Ala Asn Gly Ala Thr Gly Pro Gly Ser Arg  
85 90 95  
Asp Pro Ala Gln Val Lys Leu Leu Pro Gly Arg His Met Leu Phe Pro  
100 105 110

197/518

Pro Leu Glu Arg Val His Tyr Leu Gln Val Pro Leu Ser Arg Arg Leu  
 115 120 125  
 Ser His Asp Glu Thr Asn Ile Phe Ser Thr Pro Arg Glu Pro Gly Ser  
 130 135 140  
 Phe Leu His Lys Trp Ser Ser Ser Asp Asp Ile Arg Val Leu Pro Ala  
 145 150 155 160  
 Gln Ser Arg Ala Leu Gly Gly Pro Pro Glu Tyr Leu Gly Gln Arg His  
 165 170 175  
 Arg Leu Glu Asp Glu Glu Asp Glu Glu Glu Ala Glu Gly Gly Gly Leu  
 180 185 190  
 Ala Ser Leu Arg Gln Phe Leu Glu Ser Gly Val Leu Gly Ser Gly Gly  
 195 200 205  
 Gly Pro Pro Arg Gly Pro Gly Phe Phe Arg Glu Glu Ile Thr Thr Phe  
 210 215 220  
 Ile Asp Glu Thr Pro Leu Pro Ser Pro Thr Ala Ser Pro Gly His Ser  
 225 230 235 240  
 Pro Arg Arg Pro Arg Pro Leu Gly Leu Ser Pro Arg Arg Leu Ser Leu  
 245 250 255  
 Gly Ser Pro Glu Ser Arg Ala Val Gly Leu Pro Leu Gly Leu Ser Ala  
 260 265 270  
 Gly Arg Arg Cys Ser Leu Thr Gly Gly Glu Glu Ser Ala Arg Ala Trp  
 275 280 285  
 Gly Gly Ser Trp Gly Pro Gly Asn Pro Ile Phe Pro Gln Leu Thr Leu  
 290 295 300  
 Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val  
 305 310 315 320  
 Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu  
 325 330 335  
 Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys

198/518

340	345	350
Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu		
355	360	365
Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg		
370	375	380
His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg		
385	390	395
Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val		
405	410	415
Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile		
420	425	430
Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn		
435	440	445
Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly		
450	455	460
Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val		
465	470	475
Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro		
485	490	495
Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser		
500	505	510
Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val		
515	520	525
Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn		
530	535	540

&lt;210&gt; 82

&lt;211&gt; 571

&lt;212&gt; PRT

199/518

&lt;213&gt; Human

&lt;400&gt; 82

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Met Pro Ala Asn Tyr Thr Cys Thr Arg Pro Asp Gly Asp Asn Thr Asp
      5              10              15
Phe Arg Tyr Phe Ile Tyr Ala Val Thr Tyr Thr Val Ile Leu Val Pro
      20              25              30
Gly Leu Ile Gly Asn Ile Leu Ala Leu Trp Val Phe Tyr Gly Tyr Met
      35              40              45
Lys Glu Thr Lys Arg Ala Val Ile Phe Met Ile Asn Leu Ala Ile Ala
      50              55              60
Asp Leu Leu Gln Val Leu Ser Leu Pro Leu Arg Ile Phe Tyr Tyr Leu
      65              70              75              80
Asn His Asp Trp Pro Phe Gly Pro Gly Leu Cys Met Phe Cys Phe Tyr
      85              90              95
Leu Lys Tyr Val Asn Met Tyr Ala Ser Ile Tyr Phe Leu Val Cys Ile
      100             105             110
Ser Val Arg Arg Phe Trp Phe Leu Met Tyr Pro Phe Arg Phe His Asp
      115             120             125
Cys Lys Gln Lys Tyr Asp Leu Tyr Ile Ser Ile Ala Gly Trp Leu Ile
      130             135             140
Ile Cys Leu Ala Cys Val Leu Phe Pro Leu Leu Arg Thr Ser Asp Asp
      145             150             155             160
Thr Ser Gly Asn Arg Thr Lys Cys Phe Val Asp Leu Pro Thr Arg Asn
      165             170             175
Val Asn Leu Ala Gln Ser Val Val Met Met Thr Ile Gly Glu Leu Ile
      180             185             190
Gly Phe Val Thr Pro Leu Leu Ile Val Leu Tyr Cys Thr Trp Lys Thr
      195             200             205

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200/518

Val Leu Ser Leu Gln Asp Lys Tyr Pro Met Ala Gln Asp Leu Gly Glu  
 210 215 220  
 Lys Gln Lys Ala Leu Lys Met Ile Leu Thr Cys Ala Gly Val Phe Leu  
 225 230 235 240  
 Ile Cys Phe Ala Pro Tyr His Phe Ser Phe Pro Leu Asp Phe Leu Val  
 245 250 255  
 Lys Ser Asn Glu Ile Lys Ser Cys Leu Ala Arg Arg Val Ile Leu Ile  
 260 265 270  
 Phe His Ser Val Ala Leu Cys Leu Ala Ser Leu Asn Ser Cys Leu Asp  
 275 280 285  
 Pro Val Ile Tyr Tyr Phe Ser Thr Asn Glu Phe Arg Arg Arg Leu Ser  
 290 295 300  
 Arg Gln Asp Leu His Asp Ser Ile Gln Leu His Ala Lys Ser Phe Val  
 305 310 315 320  
 Ser Asn His Thr Ala Ser Thr Met Thr Pro Glu Leu Cys Ala Ser Lys  
 325 330 335  
 Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp  
 340 345 350  
 Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly  
 355 360 365  
 Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly  
 370 375 380  
 Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly  
 385 390 395 400  
 Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe  
 405 410 415  
 Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe  
 420 425 430  
 Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu

201/518

435	440	445	
Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys			
450	455	460	
Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser			
465	470	475	480
His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val			
485	490	495	
Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala			
500	505	510	
Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu			
515	520	525	
Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro			
530	535	540	
Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala			
545	550	555	560
Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn			
565	570		

&lt;210&gt; 83

&lt;211&gt; 577

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 83

Met Asn Gly Leu Glu Val Ala Pro Pro Gly Leu Ile Thr Asn Phe Ser
5 10 15
Leu Ala Thr Ala Glu Gln Cys Gly Gln Glu Thr Pro Leu Glu Asn Met
20 25 30
Leu Phe Ala Ser Phe Tyr Leu Leu Asp Phe Ile Leu Ala Leu Val Gly

202/518

35	40	45
Asn Thr Leu Ala Leu Trp Leu Phe Ile Arg Asp His Lys Ser Gly Thr		
50	55	60
Pro Ala Asn Val Phe Leu Met His Leu Ala Val Ala Asp Leu Ser Cys		
65	70	75
Val Leu Val Leu Pro Thr Arg Leu Val Tyr His Phe Ser Gly Asn His		
85	90	95
Trp Pro Phe Gly Glu Ile Ala Cys Arg Leu Thr Gly Phe Leu Phe Tyr		
100	105	110
Leu Asn Met Tyr Ala Ser Ile Tyr Phe Leu Thr Cys Ile Ser Ala Asp		
115	120	125
Arg Phe Leu Ala Ile Val His Pro Val Lys Ser Leu Lys Leu Arg Arg		
130	135	140
Pro Leu Tyr Ala His Leu Ala Cys Ala Phe Leu Trp Val Val Val Ala		
145	150	155
Val Ala Met Ala Pro Leu Leu Val Ser Pro Gln Thr Val Gln Thr Asn		
165	170	175
His Thr Val Val Cys Leu Gln Leu Tyr Arg Glu Lys Ala Ser His His		
180	185	190
Ala Leu Val Ser Leu Ala Val Ala Phe Thr Phe Pro Phe Ile Thr Thr		
195	200	205
Val Thr Cys Tyr Leu Leu Ile Ile Arg Ser Leu Arg Gln Gly Leu Arg		
210	215	220
Val Glu Lys Arg Leu Lys Thr Lys Ala Val Arg Met Ile Ala Ile Val		
225	230	235
Leu Ala Ile Phe Leu Val Cys Phe Val Pro Tyr His Val Asn Arg Ser		
245	250	255
Val Tyr Val Leu His Tyr Arg Ser His Gly Ala Ser Cys Ala Thr Gln		
260	265	270

203/518

Arg Ile Leu Ala Leu Ala Asn Arg Ile Thr Ser Cys Leu Thr Ser Leu  
 275 280 285  
 Asn Gly Ala Leu Asp Pro Ile Met Tyr Phe Phe Val Ala Glu Lys Phe  
 290 295 300  
 Arg His Ala Leu Cys Asn Leu Leu Cys Gly Lys Arg Leu Lys Gly Pro  
 305 310 315 320  
 Pro Pro Ser Phe Glu Gly Lys Thr Asn Glu Ser Ser Leu Ser Ala Lys  
 325 330 335  
 Ser Glu Leu Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro  
 340 345 350  
 Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val  
 355 360 365  
 Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys  
 370 375 380  
 Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val  
 385 390 395 400  
 Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His  
 405 410 415  
 Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val  
 420 425 430  
 Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg  
 435 440 445  
 Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu  
 450 455 460  
 Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu  
 465 470 475 480  
 Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln  
 485 490 495  
 Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp



204/518

500	505	510
Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly		
515	520	525
Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser		
530	535	540
Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu		
545	550	555
Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr		
565	570	575

Asn

&lt;210&gt; 84

&lt;211&gt; 547

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 84

Met Asn Gly Thr Tyr Asn Thr Cys Gly Ser Ser Asp Leu Thr Trp Pro		
5	10	15
Pro Ala Ile Lys Leu Gly Phe Tyr Ala Tyr Leu Gly Val Leu Leu Val		
20	25	30
Leu Gly Leu Leu Leu Asn Ser Leu Ala Leu Trp Val Phe Cys Cys Arg		
35	40	45
Met Gln Gln Trp Thr Glu Thr Arg Ile Tyr Met Thr Asn Leu Ala Val		
50	55	60
Ala Asp Leu Cys Leu Leu Cys Thr Leu Pro Phe Val Leu His Ser Leu		
65	70	75
Arg Asp Thr Ser Asp Thr Pro Leu Cys Gln Leu Ser Gln Gly Ile Tyr		
85	90	95

205/518

Leu Thr Asn Arg Tyr Met Ser Ile Ser Leu Val Thr Ala Ile Ala Val			
100	105	110	
Asp Arg Tyr Val Ala Val Arg His Pro Leu Arg Ala Arg Gly Leu Arg			
115	120	125	
Ser Pro Arg Gln Ala Ala Ala Val Cys Ala Val Leu Trp Val Leu Val			
130	135	140	
Ile Gly Ser Leu Val Ala Arg Trp Leu Leu Gly Ile Gln Glu Gly Gly			
145	150	155	160
Phe Cys Phe Arg Ser Thr Arg His Asn Phe Asn Ser Met Ala Phe Pro			
165	170	175	
Leu Leu Gly Phe Tyr Leu Pro Leu Ala Val Val Val Phe Cys Ser Leu			
180	185	190	
Lys Val Val Thr Ala Leu Ala Gln Arg Pro Pro Thr Asp Val Gly Gln			
195	200	205	
Ala Glu Ala Thr Arg Lys Ala Ala Arg Met Val Trp Ala Asn Leu Leu			
210	215	220	
Val Phe Val Val Cys Phe Leu Pro Leu His Val Gly Leu Thr Val Arg			
225	230	235	240
Leu Ala Val Gly Trp Asn Ala Cys Ala Leu Leu Glu Thr Ile Arg Arg			
245	250	255	
Ala Leu Tyr Ile Thr Ser Lys Leu Ser Asp Ala Asn Cys Cys Leu Asp			
260	265	270	
Ala Ile Cys Tyr Tyr Tyr Met Ala Lys Glu Phe Gln Glu Ala Ser Ala			
275	280	285	
Leu Ala Val Ala Pro Arg Ala Lys Ala His Lys Ser Gln Asp Ser Leu			
290	295	300	
Cys Val Thr Leu Ala Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val			
305	310	315	320
Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe			

206/518

	325		330		335
Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr					
	340		345		350
Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr					
	355		360		365
Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro					
	370		375		380
Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly					
385		390		395	400
Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys					
	405		410		415
Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile					
	420		425		430
Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His					
	435		440		445
Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp					
	450		455		460
Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile					
465		470		475	480
Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro					
	485		490		495
Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr					
	500		505		510
Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val					
	515		520		525
Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu					
	530		535		540
Leu Tyr Asn					
545					

207/518

&lt;210&gt; 85

&lt;211&gt; 679

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 85

Met Ala Ile His Lys Ala Leu Val Met Cys Leu Gly Leu Pro Leu Phe  
5 10 15  
Leu Phe Pro Gly Ala Trp Ala Gln Gly His Val Pro Pro Gly Cys Ser  
20 25 30  
Gln Gly Leu Asn Pro Leu Tyr Tyr Asn Leu Cys Asp Arg Ser Gly Ala  
35 40 45  
Trp Gly Ile Val Leu Glu Ala Val Ala Gly Ala Gly Ile Val Thr Thr  
50 55 60  
Phe Val Leu Thr Ile Ile Leu Val Ala Ser Leu Pro Phe Val Gln Asp  
65 70 75 80  
Thr Lys Lys Arg Ser Leu Leu Gly Thr Gln Val Phe Phe Leu Leu Gly  
85 90 95  
Thr Leu Gly Leu Phe Cys Leu Val Phe Ala Cys Val Val Lys Pro Asp  
100 105 110  
Phe Ser Thr Cys Ala Ser Arg Arg Phe Leu Phe Gly Val Leu Phe Ala  
115 120 125  
Ile Cys Phe Ser Cys Leu Ala Ala His Val Phe Ala Leu Asn Phe Leu  
130 135 140  
Ala Arg Lys Asn His Gly Pro Arg Gly Trp Val Ile Phe Thr Val Ala  
145 150 155 160  
Leu Leu Leu Thr Leu Val Glu Val Ile Ile Asn Thr Glu Trp Leu Ile  
165 170 175

208/518

Ile Thr Leu Val Arg Gly Ser Gly Glu Gly Gly Pro Gln Gly Asn Ser  
 180 185 190  
 Ser Ala Gly Trp Ala Val Ala Ser Pro Cys Ala Ile Ala Asn Met Asp  
 195 200 205  
 Phe Val Met Ala Leu Ile Tyr Val Met Leu Leu Leu Leu Gly Ala Phe  
 210 215 220  
 Leu Gly Ala Trp Pro Ala Leu Cys Gly Arg Tyr Lys Arg Trp Arg Lys  
 225 230 235 240  
 His Gly Val Phe Val Leu Leu Thr Thr Ala Thr Ser Val Ala Ile Trp  
 245 250 255  
 Val Val Trp Ile Val Met Tyr Thr Tyr Gly Asn Lys Gln His Asn Ser  
 260 265 270  
 Pro Thr Trp Asp Asp Pro Thr Leu Ala Ile Ala Leu Ala Ala Asn Ala  
 275 280 285  
 Trp Ala Phe Val Leu Phe Tyr Val Ile Pro Glu Val Ser Gln Val Thr  
 290 295 300  
 Lys Ser Ser Pro Glu Gln Ser Tyr Gln Gly Asp Met Tyr Pro Thr Arg  
 305 310 315 320  
 Gly Val Gly Tyr Glu Thr Ile Leu Lys Glu Gln Lys Gly Gln Ser Met  
 325 330 335  
 Phe Val Glu Asn Lys Ala Phe Ser Met Asp Glu Pro Val Ala Ala Lys  
 340 345 350  
 Arg Pro Val Ser Pro Tyr Ser Gly Tyr Asn Gly Gln Leu Leu Thr Ser  
 355 360 365  
 Val Tyr Gln Pro Thr Glu Met Ala Leu Met His Lys Val Pro Ser Glu  
 370 375 380  
 Gly Ala Tyr Asp Ile Ile Leu Pro Arg Ala Thr Ala Asn Ser Gln Val  
 385 390 395 400  
 Met Gly Ser Ala Asn Ser Thr Leu Arg Ala Glu Asp Met Tyr Ser Ala

209/518

405	410	415
Gln Ser His Gln Ala Ala Thr Pro Pro Lys Asp Gly Lys Asn Ser Gln		
420	425	430
Val Phe Arg Asn Pro Tyr Val Trp Asp Ala Ser Lys Gly Glu Glu Leu		
435	440	445
Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn		
450	455	460
Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr		
465	470	475
Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val		
485	490	495
Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe		
500	505	510
Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala		
515	520	525
Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp		
530	535	540
Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu		
545	550	555
Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn		
565	570	575
Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr		
580	585	590
Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr		
595	600	605
Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln		
610	615	620
Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His		
625	630	635
		640

210/518

Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg  
                     645                    650                    655  
 Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His  
                     660                    665                    670  
 Gly Met Asp Glu Leu Tyr Asn  
                     675

&lt;210&gt; 86

&lt;211&gt; 625

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 86

Met Asn Arg His His Leu Gln Asp His Phe Leu Glu Ile Asp Lys Lys  
                     5                    10                    15  
 Asn Cys Cys Val Phe Arg Asp Asp Phe Ile Ala Lys Val Leu Pro Pro  
                     20                    25                    30  
 Val Leu Gly Leu Glu Phe Ile Phe Gly Leu Leu Gly Asn Gly Leu Ala  
                     35                    40                    45  
 Leu Trp Ile Phe Cys Phe His Leu Lys Ser Trp Lys Ser Ser Arg Ile  
                     50                    55                    60  
 Phe Leu Phe Asn Leu Ala Val Ala Asp Phe Leu Leu Ile Ile Cys Leu  
                     65                    70                    75                    80  
 Pro Phe Val Met Asp Tyr Tyr Val Arg Arg Ser Asp Trp Lys Phe Gly  
                     85                    90                    95  
 Asp Ile Pro Cys Arg Leu Val Leu Phe Met Phe Ala Met Asn Arg Gln  
                     100                    105                    110  
 Gly Ser Ile Ile Phe Leu Thr Val Val Ala Val Asp Arg Tyr Phe Arg  
                     115                    120                    125

211/518

Val Val His Pro His His Ala Leu Asn Lys Ile Ser Asn Trp Thr Ala

130

135

140

Ala Ile Ile Ser Cys Leu Leu Trp Gly Ile Thr Val Gly Leu Thr Val

145

150

155

160

His Leu Leu Lys Lys Lys Leu Leu Ile Gln Asn Gly Pro Ala Asn Val

165

170

175

Cys Ile Ser Phe Ser Ile Cys His Thr Phe Arg Trp His Glu Ala Met

180

185

190

Phe Leu Leu Glu Phe Leu Leu Pro Leu Gly Ile Ile Leu Phe Cys Ser

195

200

205

Ala Arg Ile Ile Trp Ser Leu Arg Gln Arg Gln Met Asp Arg His Ala

210

215

220

Lys Ile Lys Arg Ala Ile Thr Phe Ile Met Val Val Ala Ile Val Phe

225

230

235

240

Val Ile Cys Phe Leu Pro Ser Val Val Val Arg Ile Arg Ile Phe Trp

245

250

255

Leu Leu His Thr Ser Gly Thr Gln Asn Cys Glu Val Tyr Arg Ser Val

260

265

270

Asp Leu Ala Phe Phe Ile Thr Leu Ser Phe Thr Tyr Met Asn Ser Met

275

280

285

Leu Asp Pro Val Val Tyr Tyr Phe Ser Ser Pro Ser Phe Pro Asn Phe

290

295

300

Phe Ser Thr Leu Ile Asn Arg Cys Leu Gln Arg Lys Met Thr Gly Glu

305

310

315

320

Pro Asp Asn Asn Arg Ser Thr Ser Val Glu Leu Thr Gly Asp Pro Asn

325

330

335

Lys Thr Arg Gly Ala Pro Glu Ala Leu Met Ala Asn Ser Gly Glu Pro

340

345

350

Trp Ser Pro Ser Tyr Leu Gly Pro Thr Ser Asn Asn His Ser Lys Lys



212/518

355	360	365
Gly His Cys His Gln Glu Pro Ala Ser Leu Glu Lys Gln Leu Gly Cys		
370	375	380
Cys Ile Glu Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro		
385	390	395
Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val		
405	410	415
Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys		
420	425	430
Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val		
435	440	445
Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His		
450	455	460
Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val		
465	470	475
Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg		
485	490	495
Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu		
500	505	510
Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu		
515	520	525
Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln		
530	535	540
Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp		
545	550	555
Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly		
565	570	575
Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser		
580	585	590

213/518

Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu

595

600

605

Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr

610

615

620

Asn

625

&lt;210&gt; 87

&lt;211&gt; 778

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 87

Met Asn Ser Thr Gly His Leu Gln Asp Ala Pro Asn Ala Thr Ser Leu

5

10

15

His Val Pro His Ser Gln Glu Gly Asn Ser Thr Ser Leu Gln Glu Gly

20

25

30

Leu Gln Asp Leu Ile His Thr Ala Thr Leu Val Thr Cys Thr Phe Leu

35

40

45

Leu Ala Val Ile Phe Cys Leu Gly Ser Tyr Gly Asn Phe Ile Val Phe

50

55

60

Leu Ser Phe Phe Asp Pro Ala Phe Arg Lys Phe Arg Thr Asn Phe Asp

65

70

75

80

Phe Met Ile Leu Asn Leu Ser Phe Cys Asp Leu Phe Ile Cys Gly Val

85

90

95

Thr Ala Pro Met Phe Thr Phe Val Leu Phe Phe Ser Ser Ala Ser Ser

100

105

110

Ile Pro Asp Ala Phe Cys Phe Thr Phe His Leu Thr Ser Ser Gly Phe

115

120

125

214/518

Ile Ile Met Ser Leu Lys Thr Val Ala Val Ile Ala Leu His Arg Leu  
 130 135 140  
 Arg Met Val Leu Gly Lys Gln Pro Asn Arg Thr Ala Ser Phe Pro Cys  
 145 150 155 160  
 Thr Val Leu Leu Thr Leu Leu Leu Trp Ala Thr Ser Phe Thr Leu Ala  
 165 170 175  
 Thr Leu Ala Thr Leu Lys Thr Ser Lys Ser His Leu Cys Leu Pro Met  
 180 185 190  
 Ser Ser Leu Ile Ala Gly Lys Gly Lys Ala Ile Leu Ser Leu Tyr Val  
 195 200 205  
 Val Asp Phe Thr Phe Cys Val Ala Val Val Ser Val Ser Tyr Ile Met  
 210 215 220  
 Ile Ala Gln Thr Leu Arg Lys Asn Ala Gln Val Arg Lys Cys Pro Pro  
 225 230 235 240  
 Val Ile Thr Val Asp Ala Ser Arg Pro Gln Pro Phe Met Gly Val Pro  
 245 250 255  
 Val Gln Gly Gly Gly Asp Pro Ile Gln Cys Ala Met Pro Ala Leu Tyr  
 260 265 270  
 Arg Asn Gln Asn Tyr Asn Lys Leu Gln His Val Gln Thr Arg Gly Tyr  
 275 280 285  
 Thr Lys Ser Pro Asn Gln Leu Val Thr Pro Ala Ala Ser Arg Leu Gln  
 290 295 300  
 Leu Val Ser Ala Ile Asn Leu Ser Thr Ala Lys Asp Ser Lys Ala Val  
 305 310 315 320  
 Val Thr Cys Val Ile Ile Val Leu Ser Val Leu Val Cys Cys Leu Pro  
 325 330 335  
 Leu Gly Ile Ser Leu Val Gln Val Val Leu Ser Ser Asn Gly Ser Phe  
 340 345 350  
 Ile Leu Tyr Gln Phe Glu Leu Phe Gly Phe Thr Leu Ile Phe Phe Lys

215/518

355	360	365
Ser Gly Leu Asn Pro Phe Ile Tyr Ser Arg Asn Ser Ala Gly Leu Arg		
370	375	380
Arg Lys Val Leu Trp Cys Leu Gln Tyr Ile Gly Leu Gly Phe Phe Cys		
385	390	395
Cys Lys Gln Lys Thr Arg Leu Arg Ala Met Gly Lys Gly Asn Leu Glu		
405	410	415
Val Asn Arg Asn Lys Ser Ser His His Glu Thr Asn Ser Ala Tyr Met		
420	425	430
Leu Ser Pro Lys Pro Gln Lys Lys Phe Val Asp Gln Ala Cys Gly Pro		
435	440	445
Ser His Ser Lys Glu Ser Met Val Ser Pro Lys Ile Ser Ala Gly His		
450	455	460
Gln His Cys Gly Gln Ser Ser Ser Thr Pro Ile Asn Thr Arg Ile Glu		
465	470	475
Pro Tyr Tyr Ser Ile Tyr Asn Ser Ser Pro Ser Gln Glu Glu Ser Ser		
485	490	495
Pro Cys Asn Leu Gln Pro Val Asn Ser Phe Gly Phe Ala Asn Ser Tyr		
500	505	510
Ile Ala Met His Tyr His Thr Thr Asn Asp Leu Val Gln Glu Tyr Asp		
515	520	525
Ser Thr Ser Ala Lys Gln Ile Pro Val Pro Ser Val Ala Ser Lys Gly		
530	535	540
Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly		
545	550	555
Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp		
565	570	575
Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys		
580	585	590

216/518

Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val  
           595                          600                          605  
 Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe  
           610                          615                          620  
 Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe  
   625                          630                          635                          640  
 Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly  
                           645                          650                          655  
 Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu  
           660                          665                          670  
 Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His  
           675                          680                          685  
 Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn  
           690                          695                          700  
 Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp  
   705                          710                          715                          720  
 His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro  
                           725                          730                          735  
 Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn  
           740                          745                          750  
 Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly  
           755                          760                          765  
 Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
           770                          775

&lt;210&gt; 88

&lt;211&gt; 584

&lt;212&gt; PRT

&lt;213&gt; Human

217/518

&lt;400&gt; 88

Met Tyr Asn Gly Ser Cys Cys Arg Ile Glu Gly Asp Thr Ile Ser Gln  
                   5                  10                  15  
 Val Met Pro Pro Leu Leu Ile Val Ala Phe Val Leu Gly Ala Leu Gly  
                   20                  25                  30  
 Asn Gly Val Ala Leu Cys Gly Phe Cys Phe His Met Lys Thr Trp Lys  
                   35                  40                  45  
 Pro Ser Thr Val Tyr Leu Phe Asn Leu Ala Val Ala Asp Phe Leu Leu  
                   50                  55                  60  
 Met Ile Cys Leu Pro Phe Arg Thr Asp Tyr Tyr Leu Arg Arg Arg His  
                   65                  70                  75                  80  
 Trp Ala Phe Gly Asp Ile Pro Cys Arg Val Gly Leu Phe Thr Leu Ala  
                   85                  90                  95  
 Met Asn Arg Ala Gly Ser Ile Val Phe Leu Thr Val Val Ala Ala Asp  
                   100                  105                  110  
 Arg Tyr Phe Lys Val Val His Pro His His Ala Val Asn Thr Ile Ser  
                   115                  120                  125  
 Thr Arg Val Ala Ala Gly Ile Val Cys Thr Leu Trp Ala Leu Val Ile  
                   130                  135                  140  
 Leu Gly Thr Val Tyr Leu Leu Leu Glu Asn His Leu Cys Val Gln Glu  
                   145                  150                  155                  160  
 Thr Ala Val Ser Cys Glu Ser Phe Ile Met Glu Ser Ala Asn Gly Trp  
                   165                  170                  175  
 His Asp Ile Met Phe Gln Leu Glu Phe Phe Met Pro Leu Gly Ile Ile  
                   180                  185                  190  
 Leu Phe Cys Ser Phe Lys Ile Val Trp Ser Leu Arg Arg Arg Gln Gln  
                   195                  200                  205  
 Leu Ala Arg Gln Ala Arg Met Lys Lys Ala Thr Arg Phe Ile Met Val

218/518

210	215	220
Val Ala Ile Val Phe Ile Thr Cys Tyr Leu Pro Ser Val Ser Ala Arg		
225	230	235
Leu Tyr Phe Leu Trp Thr Val Pro Ser Ser Ala Cys Asp Pro Ser Val		
245	250	255
His Gly Ala Leu His Ile Thr Leu Ser Phe Thr Tyr Met Asn Ser Met		
260	265	270
Leu Asp Pro Leu Val Tyr Tyr Phe Ser Ser Pro Ser Phe Pro Lys Phe		
275	280	285
Tyr Asn Lys Leu Lys Ile Cys Ser Leu Lys Pro Lys Gln Pro Gly His		
290	295	300
Ser Lys Thr Gln Arg Pro Glu Glu Met Pro Ile Ser Asn Leu Gly Arg		
305	310	315
Arg Ser Cys Ile Ser Val Ala Asn Ser Phe Gln Ser Gln Ser Asp Gly		
325	330	335
Gln Trp Asp Pro His Ile Val Glu Trp His Ala Ser Lys Gly Glu Glu		
340	345	350
Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val		
355	360	365
Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr		
370	375	380
Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro		
385	390	395
Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys		
405	410	415
Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser		
420	425	430
Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp		
435	440	445

219/518

Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr  
 450 455 460  
 Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly  
 465 470 475 480  
 Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val  
 485 490 495  
 Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys  
 500 505 510  
 Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr  
 515 520 525  
 Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn  
 530 535 540  
 His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys  
 545 550 555 560  
 Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr  
 565 570 575  
 His Gly Met Asp Glu Leu Tyr Asn  
 580

&lt;210&gt; 89

&lt;211&gt; 585

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 89

Met Gly Asp Glu Leu Ala Pro Cys Pro Val Gly Thr Thr Ala Trp Pro  
 5 10 15  
 Ala Leu Ile Gln Leu Ile Ser Lys Thr Pro Cys Met Pro Gln Ala Ala  
 20 25 30



220/518

Ser Asn Thr Ser Leu Gly Leu Gly Asp Leu Arg Val Pro Ser Ser Met  
 35 40 45  
 Leu Tyr Trp Leu Phe Leu Pro Ser Ser Leu Leu Ala Ala Ala Thr Leu  
 50 55 60  
 Ala Val Ser Pro Leu Leu Leu Val Thr Ile Leu Arg Asn Gln Arg Leu  
 65 70 75 80  
 Arg Gln Glu Pro His Tyr Leu Leu Pro Ala Asn Ile Leu Leu Ser Asp  
 85 90 95  
 Leu Ala Tyr Ile Leu Leu His Met Leu Ile Ser Ser Ser Ser Leu Gly  
 100 105 110  
 Gly Trp Glu Leu Gly Arg Met Ala Cys Gly Ile Leu Thr Asp Ala Val  
 115 120 125  
 Phe Ala Ala Cys Thr Ser Thr Ile Leu Ser Phe Thr Ala Ile Val Leu  
 130 135 140  
 His Thr Tyr Leu Ala Val Ile His Pro Leu Arg Tyr Leu Ser Phe Met  
 145 150 155 160  
 Ser His Gly Ala Ala Trp Lys Ala Val Ala Leu Ile Trp Leu Val Ala  
 165 170 175  
 Cys Cys Phe Pro Thr Phe Leu Ile Trp Leu Ser Lys Trp Gln Asp Ala  
 180 185 190  
 Gln Leu Glu Glu Gln Gly Ala Ser Tyr Ile Leu Pro Pro Ser Met Gly  
 195 200 205  
 Thr Gln Pro Gly Cys Gly Leu Leu Val Ile Val Thr Tyr Thr Ser Ile  
 210 215 220  
 Leu Cys Val Leu Phe Leu Cys Thr Ala Leu Ile Ala Asn Cys Phe Trp  
 225 230 235 240  
 Arg Ile Tyr Ala Glu Ala Lys Thr Ser Gly Ile Trp Gly Gln Gly Tyr  
 245 250 255  
 Ser Arg Ala Arg Gly Thr Leu Leu Ile His Ser Val Leu Ile Thr Leu

221/518

260	265	270
Tyr Val Ser Thr Gly Val Val Phe Ser Leu Asp Met Val Leu Thr Arg		
275	280	285
Tyr His His Ile Asp Ser Gly Thr His Thr Trp Leu Leu Ala Ala Asn		
290	295	300
Ser Glu Val Leu Met Met Leu Pro Arg Ala Met Leu Pro Tyr Leu Tyr		
305	310	315
Leu Leu Arg Tyr Arg Gln Leu Leu Gly Met Val Arg Gly His Leu Pro		
325	330	335
Ser Arg Arg His Gln Ala Ile Phe Thr Ile Ser Ala Ser Lys Gly Glu		
340	345	350
Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp		
355	360	365
Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala		
370	375	380
Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu		
385	390	395
Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln		
405	410	415
Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys		
420	425	430
Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys		
435	440	445
Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp		
450	455	460
Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp		
465	470	475
Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn		
485	490	495

222/518

Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe

500

505

510

Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His

515

520

525

Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp

530

535

540

Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu

545

550

555

560

Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile

565

570

575

Thr His Gly Met Asp Glu Leu Tyr Asn

580

585

&lt;210&gt; 90

&lt;211&gt; 611

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 90

Met Arg Met Glu Asp Glu Asp Tyr Asn Thr Ser Ile Ser Tyr Gly Asp

5

10

15

Glu Tyr Pro Asp Tyr Leu Asp Ser Ile Val Val Leu Glu Asp Leu Ser

20

25

30

Pro Leu Glu Ala Arg Val Thr Arg Ile Phe Leu Val Val Val Tyr Ser

35

40

45

Ile Val Cys Phe Leu Gly Ile Leu Gly Asn Gly Leu Val Ile Ile Ile

50

55

60

Ala Thr Phe Lys Met Lys Lys Thr Val Asn Met Val Trp Phe Leu Asn

65

70

75

80

223/518

Leu Ala Val Ala Asp Phe Leu Phe Asn Val Phe Leu Pro Ile His Ile  
                             85                            90                            95  
 Thr Tyr Ala Ala Met Asp Tyr His Trp Val Phe Gly Thr Ala Met Cys  
                             100                            105                            110  
 Lys Ile Ser Asn Phe Leu Leu Ile His Asn Met Phe Thr Ser Val Phe  
                             115                            120                            125  
 Leu Leu Thr Ile Ile Ser Ser Asp Arg Cys Ile Ser Val Leu Leu Pro  
                             130                            135                            140  
 Val Trp Ser Gln Asn His Arg Ser Val Arg Leu Ala Tyr Met Ala Cys  
 145                            150                            155                            160  
 Met Val Ile Trp Val Leu Ala Phe Phe Leu Ser Ser Pro Ser Leu Val  
                             165                            170                            175  
 Phe Arg Asp Thr Ala Asn Leu His Gly Lys Ile Ser Cys Phe Asn Asn  
                             180                            185                            190  
 Phe Ser Leu Ser Thr Pro Gly Ser Ser Ser Trp Pro Thr His Ser Gln  
                             195                            200                            205  
 Met Asp Pro Val Gly Tyr Ser Arg His Met Val Val Thr Val Thr Arg  
                             210                            215                            220  
 Phe Leu Cys Gly Phe Leu Val Pro Val Leu Ile Ile Thr Ala Cys Tyr  
 225                            230                            235                            240  
 Leu Thr Ile Val Cys Lys Leu Gln Arg Asn Arg Leu Ala Lys Thr Lys  
                             245                            250                            255  
 Lys Pro Phe Lys Ile Ile Val Thr Ile Ile Ile Thr Phe Phe Leu Cys  
                             260                            265                            270  
 Trp Cys Pro Tyr His Thr Leu Asn Leu Leu Glu Leu His His Thr Ala  
                             275                            280                            285  
 Met Pro Gly Ser Val Phe Ser Leu Gly Leu Pro Leu Ala Thr Ala Leu  
                             290                            295                            300  
 Ala Ile Ala Asn Ser Cys Met Asn Pro Ile Leu Tyr Val Phe Met Gly

224/518

305	310	315	320
Gln Asp Phe Lys Lys Phe Lys Val Ala Leu Phe Ser Arg Leu Val Asn			
325	330	335	
Ala Leu Ser Glu Asp Thr Gly His Ser Ser Tyr Pro Ser His Arg Ser			
340	345	350	
Phe Thr Lys Met Ser Ser Met Asn Glu Arg Thr Ser Met Asn Glu Arg			
355	360	365	
Glu Thr Gly Met Leu Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val			
370	375	380	
Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe			
385	390	395	400
Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr			
405	410	415	
Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr			
420	425	430	
Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro			
435	440	445	
Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly			
450	455	460	
Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys			
465	470	475	480
Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile			
485	490	495	
Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His			
500	505	510	
Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp			
515	520	525	
Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile			
530	535	540	

225/518

Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro  
 545                      550                      555                      560  
 Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr  
                          565                      570                      575  
 Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val  
                          580                      585                      590  
 Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu  
                          595                      600                      605  
 Leu Tyr Asn  
                          610

&lt;210&gt; 91

&lt;211&gt; 591

&lt;212&gt; PRT

&lt;213&gt; Rat

&lt;400&gt; 91

Met Glu Val Ser Arg Glu Met Leu Phe Glu Glu Leu Asp Asn Tyr Ser  
                          5                      10                      15  
 Tyr Ala Leu Glu Tyr Tyr Ser Gln Glu Pro Asp Ala Glu Glu Asn Val  
                          20                      25                      30  
 Tyr Pro Gly Ile Val His Trp Ile Ser Leu Leu Leu Tyr Ala Leu Ala  
                          35                      40                      45  
 Phe Val Leu Gly Ile Pro Gly Asn Ala Ile Val Ile Trp Phe Met Gly  
                          50                      55                      60  
 Phe Lys Trp Lys Lys Thr Val Thr Thr Leu Trp Phe Leu Asn Leu Ala  
                          65                      70                      75                      80  
 Ile Ala Asp Phe Val Phe Val Leu Phe Leu Pro Leu Tyr Ile Ser Tyr  
                          85                      90                      95

226/518

Val	Ala	Leu	Ser	Phe	His	Trp	Pro	Phe	Gly	Arg	Trp	Leu	Cys	Lys	Leu
		100						105					110		
Asn	Ser	Phe	Ile	Ala	Gln	Leu	Asn	Met	Phe	Ser	Ser	Val	Phe	Phe	Leu
		115				120						125			
Thr	Val	Ile	Ser	Leu	Asp	Arg	Tyr	Ile	His	Leu	Ile	His	Pro	Gly	Leu
	130					135					140				
Ser	His	Pro	His	Arg	Thr	Leu	Lys	Asn	Ser	Leu	Leu	Val	Val	Leu	Phe
145				150					155					160	
Val	Trp	Leu	Leu	Ala	Ser	Leu	Leu	Gly	Gly	Pro	Thr	Leu	Tyr	Phe	Arg
			165					170					175		
Asp	Thr	Val	Glu	Val	Asn	Asn	Arg	Ile	Ile	Cys	Tyr	Asn	Asn	Phe	Gln
		180					185						190		
Glu	Tyr	Glu	Leu	Thr	Leu	Met	Arg	His	His	Val	Leu	Thr	Trp	Val	Lys
	195					200						205			
Phe	Leu	Phe	Gly	Tyr	Leu	Leu	Pro	Leu	Leu	Thr	Met	Ser	Ser	Cys	Tyr
	210					215					220				
Leu	Cys	Leu	Ile	Phe	Lys	Thr	Lys	Lys	Gln	Asn	Ile	Leu	Ile	Ser	Ser
225				230					235					240	
Lys	His	Leu	Trp	Met	Ile	Leu	Ser	Val	Val	Ile	Ala	Phe	Met	Val	Cys
			245					250				255			
Trp	Thr	Pro	Phe	His	Leu	Phe	Ser	Ile	Trp	Glu	Leu	Ser	Ile	His	His
		260					265					270			
Asn	Ser	Ser	Phe	Gln	Asn	Val	Leu	Gln	Gly	Gly	Ile	Pro	Leu	Ser	Thr
		275					280					285			
Gly	Leu	Ala	Phe	Leu	Asn	Ser	Cys	Leu	Asn	Pro	Ile	Leu	Tyr	Val	Leu
	290					295					300				
Ile	Ser	Lys	Lys	Phe	Gln	Ala	Arg	Phe	Arg	Ala	Ser	Val	Ala	Glu	Val
305				310					315					320	
Leu	Lys	Arg	Ser	Leu	Trp	Glu	Ala	Ser	Cys	Ser	Gly	Thr	Val	Ser	Glu

227/518

325	330	335
Gln Leu Arg Ser Ala Glu Thr Lys Ser Leu Ser Leu Leu Glu Thr Ala		
340	345	350
Gln Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu		
355	360	365
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly		
370	375	380
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile		
385	390	395
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr		
405	410	415
Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys		
420	425	430
Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu		
435	440	445
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu		
450	455	460
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly		
465	470	475
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr		
485	490	495
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn		
500	505	510
Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser		
515	520	525
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly		
530	535	540
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu		
545	550	555
		560



228/518

Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe

565

570

575

Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn

580

585

590

&lt;210&gt; 92

&lt;211&gt; 568

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 92

Met Met Trp Gly Ala Gly Ser Pro Leu Ala Trp Leu Ser Ala Gly Ser

5

10

15

Gly Asn Val Asn Val Ser Ser Val Gly Pro Ala Glu Gly Pro Thr Gly

20

25

30

Pro Ala Ala Pro Leu Pro Ser Pro Lys Ala Trp Asp Val Val Leu Cys

35

40

45

Ile Ser Gly Thr Leu Val Ser Cys Glu Asn Ala Leu Val Val Ala Ile

50

55

60

Ile Val Gly Thr Pro Ala Phe Arg Ala Pro Met Phe Leu Leu Val Gly

65

70

75

80

Ser Leu Ala Val Ala Asp Leu Leu Ala Gly Leu Gly Leu Val Leu His

85

90

95

Phe Ala Ala Val Phe Cys Ile Gly Ser Ala Glu Met Ser Leu Val Leu

100

105

110

Val Gly Val Leu Ala Met Ala Phe Thr Ala Ser Ile Gly Ser Leu Leu

115

120

125

Ala Ile Thr Val Asp Arg Tyr Leu Ser Leu Tyr Asn Ala Leu Thr Tyr

130

135

140

229/518

Tyr Ser Glu Thr Thr Val Thr Arg Thr Tyr Val Met Leu Ala Leu Val  
 145 150 155 160  
 Trp Gly Gly Ala Leu Gly Leu Gly Leu Leu Pro Val Leu Ala Trp Asn  
 165 170 175  
 Cys Leu Asp Gly Leu Thr Thr Cys Gly Val Val Tyr Pro Leu Ser Lys  
 180 185 190  
 Asn His Leu Val Val Leu Ala Ile Ala Phe Phe Met Val Phe Gly Ile  
 195 200 205  
 Met Leu Gln Leu Tyr Ala Gln Ile Cys Arg Ile Val Cys Arg His Ala  
 210 215 220  
 Gln Gln Ile Ala Leu Gln Arg His Leu Leu Pro Ala Ser His Tyr Val  
 225 230 235 240  
 Ala Thr Arg Lys Gly Ile Ala Thr Leu Ala Val Val Leu Gly Ala Phe  
 245 250 255  
 Ala Ala Cys Trp Leu Pro Phe Thr Val Tyr Cys Leu Leu Gly Asp Ala  
 260 265 270  
 His Ser Pro Pro Leu Tyr Thr Tyr Leu Thr Leu Leu Pro Ala Thr Tyr  
 275 280 285  
 Asn Ser Met Ile Asn Pro Ile Ile Tyr Ala Phe Arg Asn Gln Asp Val  
 290 295 300  
 Gln Lys Val Leu Trp Ala Val Cys Cys Cys Cys Ser Ser Ser Lys Ile  
 305 310 315 320  
 Pro Phe Arg Ser Arg Ser Pro Ser Asp Val Ala Ser Lys Gly Glu Glu  
 325 330 335  
 Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val  
 340 345 350  
 Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr  
 355 360 365  
 Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro

230/518

370                      375                      380  
 Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys  
 385                      390                      395                      400  
 Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser  
                     405                      410                      415  
 Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp  
                     420                      425                      430  
 Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr  
                     435                      440                      445  
 Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly  
                     450                      455                      460  
 Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val  
 465                      470                      475                      480  
 Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys  
                     485                      490                      495  
 Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr  
                     500                      505                      510  
 Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn  
                     515                      520                      525  
 His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys  
                     530                      535                      540  
 Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr  
 545                      550                      555                      560  
 His Gly Met Asp Glu Leu Tyr Asn  
                     565

&lt;210&gt; 93

&lt;211&gt; 600

&lt;212&gt; PRT

231/518

&lt;213&gt; Human

&lt;400&gt; 93

Met Asn Ala Ser Ala Ala Ser Leu Asn Asp Ser Gln Val Val Val Val  
                     5                    10                    15  
 Ala Ala Glu Gly Ala Ala Ala Ala Thr Ala Ala Gly Gly Pro Asp  
                     20                    25                    30  
 Thr Gly Glu Trp Gly Pro Pro Ala Ala Ala Leu Gly Ala Gly Gly  
                     35                    40                    45  
 Gly Ala Asn Gly Ser Leu Glu Leu Ser Ser Gln Leu Ser Ala Gly Pro  
                     50                    55                    60  
 Pro Gly Leu Leu Leu Pro Ala Val Asn Pro Trp Asp Val Leu Leu Cys  
                     65                    70                    75                    80  
 Val Ser Gly Thr Val Ile Ala Gly Glu Asn Ala Leu Val Val Ala Leu  
                     85                    90                    95  
 Ile Ala Ser Thr Pro Ala Leu Arg Thr Pro Met Phe Val Leu Val Gly  
                     100                    105                    110  
 Ser Leu Ala Thr Ala Asp Leu Leu Ala Gly Cys Gly Leu Ile Leu His  
                     115                    120                    125  
 Phe Val Phe Gln Tyr Leu Val Pro Ser Glu Thr Val Ser Leu Leu Thr  
                     130                    135                    140  
 Val Gly Phe Leu Val Ala Ser Phe Ala Ala Ser Val Ser Ser Leu Leu  
                     145                    150                    155                    160  
 Ala Ile Thr Val Asp Arg Tyr Leu Ser Leu Tyr Asn Ala Leu Thr Tyr  
                     165                    170                    175  
 Tyr Ser Arg Arg Thr Leu Leu Gly Val His Leu Leu Leu Ala Ala Thr  
                     180                    185                    190  
 Trp Thr Val Ser Leu Gly Leu Gly Leu Leu Pro Val Leu Gly Trp Asn  
                     195                    200                    205

232/518

Cys Leu Ala Glu Arg Ala Ala Cys Ser Val Val Arg Pro Leu Ala Arg  
 210 215 220  
 Ser His Val Ala Leu Leu Ser Ala Ala Phe Phe Met Val Phe Gly Ile  
 225 230 235 240  
 Met Leu His Leu Tyr Val Arg Ile Cys Gln Val Val Trp Arg His Ala  
 245 250 255  
 His Gln Ile Ala Leu Gln Gln His Cys Leu Ala Pro Pro His Leu Ala  
 260 265 270  
 Ala Thr Arg Lys Gly Val Gly Thr Leu Ala Val Val Leu Gly Thr Phe  
 275 280 285  
 Gly Ala Ser Trp Leu Pro Phe Ala Ile Tyr Cys Val Val Gly Ser His  
 290 295 300  
 Glu Asp Pro Ala Val Tyr Thr Tyr Ala Thr Leu Leu Pro Ala Thr Tyr  
 305 310 315 320  
 Asn Ser Met Ile Asn Pro Ile Ile Tyr Ala Phe Arg Asn Gln Glu Ile  
 325 330 335  
 Gln Arg Ala Leu Trp Leu Leu Leu Cys Gly Cys Phe Gln Ser Lys Val  
 340 345 350  
 Pro Phe Arg Ser Arg Ser Pro Ser Glu Val Ala Ser Lys Gly Glu Glu  
 355 360 365  
 Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val  
 370 375 380  
 Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr  
 385 390 395 400  
 Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro  
 405 410 415  
 Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys  
 420 425 430  
 Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser

233/518

435	440	445
Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp		
450	455	460
Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr		
465	470	475
Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly		
485	490	495
Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val		
500	505	510
Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys		
515	520	525
Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr		
530	535	540
Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn		
545	550	555
His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys		
565	570	575
Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr		
580	585	590
His Gly Met Asp Glu Leu Tyr Asn		
595	600	

&lt;210&gt; 94

&lt;211&gt; 595

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 94

Met Ala Thr Thr Val Pro Asp Gly Cys Arg Asn Gly Leu Lys Ser Lys

234/518

	5		10		15
Tyr	Tyr	Arg	Leu	Cys	Asp
			Lys	Ala	Glu
			Ala	Trp	Gly
			Ile	Val	Leu
			Glu		
	20		25		30
Thr	Val	Ala	Thr	Ala	Gly
			Val	Val	Thr
			Ser	Val	Ala
			Phe	Met	Leu
			Thr		
	35		40		45
Leu	Pro	Ile	Leu	Val	Cys
			Lys	Val	Gln
			Asp	Ser	Asn
			Arg	Arg	Lys
			Met		
	50		55		60
Leu	Pro	Thr	Gln	Phe	Leu
			Phe	Leu	Leu
			Gly	Val	Leu
			Gly	Ile	Phe
			Gly		
	65		70		75
Leu	Thr	Phe	Ala	Phe	Ile
			Ile	Gly	Leu
			Asp	Gly	Ser
			Thr	Gly	Pro
			Thr		
	85		90		95
Arg	Phe	Phe	Leu	Phe	Gly
			Ile	Leu	Phe
			Ser	Ile	Cys
			Phe	Ser	Cys
			Leu		
	100		105		110
Leu	Ala	His	Ala	Val	Ser
			Leu	Thr	Lys
			Leu	Val	Arg
			Gly	Arg	Lys
			Pro		
	115		120		125
Leu	Ser	Leu	Leu	Val	Ile
			Leu	Gly	Leu
			Ala	Val	Gly
			Phe	Ser	Leu
			Val		
	130		135		140
Gln	Asp	Val	Ile	Ala	Ile
			Glu	Tyr	Ile
			Val	Leu	Thr
			Met	Asn	Arg
			Thr		
	145		150		155
Asn	Val	Asn	Val	Phe	Ser
			Glu	Leu	Ser
			Ala	Pro	Arg
			Arg	Asn	Glu
			Asp		
	165		170		175
Phe	Val	Leu	Leu	Leu	Thr
			Tyr	Val	Leu
			Phe	Leu	Met
			Ala	Leu	Thr
			Phe		
	180		185		190
Leu	Met	Ser	Ser	Phe	Thr
			Phe	Cys	Gly
			Ser	Phe	Thr
			Gly	Trp	Lys
			Arg		
	195		200		205
His	Gly	Ala	His	Ile	Tyr
			Leu	Thr	Met
			Leu	Leu	Ser
			Ile	Ala	Ile
			Trp		
	210		215		220
Val	Ala	Trp	Ile	Thr	Leu
			Leu	Met	Leu
			Pro	Asp	Phe
			Asp	Arg	Arg
			Trp		
	225		230		235
					240

235/518

Asp Asp Thr Ile Leu Ser Ser Ala Leu Ala Ala Asn Gly Trp Val Phe			
245	250	255	
Leu Leu Ala Tyr Val Ser Pro Glu Phe Trp Leu Leu Thr Lys Gln Arg			
260	265	270	
Asn Pro Met Asp Tyr Pro Val Glu Asp Ala Phe Cys Lys Pro Gln Leu			
275	280	285	
Val Lys Lys Ser Tyr Gly Val Glu Asn Arg Ala Tyr Ser Gln Glu Glu			
290	295	300	
Ile Thr Gln Gly Phe Glu Glu Thr Gly Asp Thr Leu Tyr Ala Pro Tyr			
305	310	315	320
Ser Thr His Phe Gln Leu Gln Asn Gln Pro Pro Gln Lys Glu Phe Ser			
325	330	335	
Ile Pro Arg Ala His Ala Trp Pro Ser Pro Tyr Lys Asp Tyr Glu Val			
340	345	350	
Lys Lys Glu Gly Ser Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val			
355	360	365	
Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe			
370	375	380	
Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr			
385	390	395	400
Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr			
405	410	415	
Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro			
420	425	430	
Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly			
435	440	445	
Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys			
450	455	460	
Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile			



236/518

465                      470                      475                      480  
 Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His  
                          485                      490                      495  
 Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp  
                          500                      505                      510  
 Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile  
                          515                      520                      525  
 Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro  
                          530                      535                      540  
 Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr  
 545                      550                      555                      560  
 Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val  
                          565                      570                      575  
 Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu  
                          580                      585                      590  
 Leu Tyr Asn  
                          595

&lt;210&gt; 95

&lt;211&gt; 657

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 95

Met Leu Ala Ala Ala Phe Ala Asp Ser Asn Ser Ser Ser Met Asn Val  
                          5                      10                      15  
 Ser Phe Ala His Leu His Phe Ala Gly Gly Tyr Leu Pro Ser Asp Ser  
                          20                      25                      30  
 Gln Asp Trp Arg Thr Ile Ile Pro Ala Leu Leu Val Ala Val Cys Leu

237/518

35	40	45
Val Gly Phe Val Gly Asn Leu Cys Val Ile Gly Ile Leu Leu His Asn		
50	55	60
Ala Trp Lys Gly Lys Pro Ser Met Ile His Ser Leu Ile Leu Asn Leu		
65	70	75
Ser Leu Ala Asp Leu Ser Leu Leu Leu Phe Ser Ala Pro Ile Arg Ala		
85	90	95
Thr Ala Tyr Ser Lys Ser Val Trp Asp Leu Gly Trp Phe Val Cys Lys		
100	105	110
Ser Ser Asp Trp Phe Ile His Thr Cys Met Ala Ala Lys Ser Leu Thr		
115	120	125
Ile Val Val Val Ala Lys Val Cys Phe Met Tyr Ala Ser Asp Pro Ala		
130	135	140
Lys Gln Val Ser Ile His Asn Tyr Thr Ile Trp Ser Val Leu Val Ala		
145	150	155
Ile Trp Thr Val Ala Ser Leu Leu Pro Leu Pro Glu Trp Phe Phe Ser		
165	170	175
Thr Ile Arg His His Glu Gly Val Glu Met Cys Leu Val Asp Val Pro		
180	185	190
Ala Val Ala Glu Glu Phe Met Ser Met Phe Gly Lys Leu Tyr Pro Leu		
195	200	205
Leu Ala Phe Gly Leu Pro Leu Phe Phe Ala Ser Phe Tyr Phe Trp Arg		
210	215	220
Ala Tyr Asp Gln Cys Lys Lys Arg Gly Thr Lys Thr Gln Asn Leu Arg		
225	230	235
Asn Gln Ile Arg Ser Lys Gln Val Thr Val Met Leu Leu Ser Ile Ala		
245	250	255
Ile Ile Ser Ala Leu Leu Trp Leu Pro Glu Trp Val Ala Trp Leu Trp		
260	265	270

238/518

Val Trp His Leu Lys Ala Ala Gly Pro Ala Pro Pro Gln Gly Phe Ile  
 275 280 285  
 Ala Leu Ser Gln Val Leu Met Phe Ser Ile Ser Ser Ala Asn Pro Leu  
 290 295 300  
 Ile Phe Leu Val Met Ser Glu Glu Phe Arg Glu Gly Leu Lys Gly Val  
 305 310 315 320  
 Trp Lys Trp Met Ile Thr Lys Lys Pro Pro Thr Val Ser Glu Ser Gln  
 325 330 335  
 Glu Thr Pro Ala Gly Asn Ser Glu Gly Leu Pro Asp Lys Val Pro Ser  
 340 345 350  
 Pro Glu Ser Pro Ala Ser Ile Pro Glu Lys Glu Lys Pro Ser Ser Pro  
 355 360 365  
 Ser Ser Gly Lys Gly Lys Thr Glu Lys Ala Glu Ile Pro Ile Leu Pro  
 370 375 380  
 Asp Val Glu Gln Phe Trp His Glu Arg Asp Thr Val Pro Ser Val Gln  
 385 390 395 400  
 Asp Asn Asp Pro Ile Pro Trp Glu His Glu Asp Gln Glu Thr Gly Glu  
 405 410 415  
 Gly Val Lys Thr Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro  
 420 425 430  
 Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val  
 435 440 445  
 Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys  
 450 455 460  
 Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val  
 465 470 475 480  
 Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His  
 485 490 495  
 Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val

239/518

500	505	510
Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg		
515	520	525
Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu		
530	535	540
Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu		
545	550	555
Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln		
565	570	575
Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp		
580	585	590
Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly		
595	600	605
Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser		
610	615	620
Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu		
625	630	635
Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr		
645	650	655
Asn		

&lt;210&gt; 96

&lt;211&gt; 657

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 96

Met Leu Ala Ala Ala Phe Ala Asp Ser Asn Ser Ser Ser Met Asn Val

5

10

15

240/518

Ser Phe Ala His Leu His Phe Ala Gly Gly Tyr Leu Pro Ser Asp Ser  
 20 25 30  
 Gln Asp Trp Arg Thr Ile Ile Pro Ala Leu Leu Val Ala Val Cys Leu  
 35 40 45  
 Val Gly Phe Val Gly Asn Leu Cys Val Ile Gly Ile Leu Leu His Asn  
 50 55 60  
 Ala Trp Lys Gly Lys Pro Ser Met Ile His Ser Leu Ile Leu Asn Leu  
 65 70 75 80  
 Ser Leu Ala Asp Leu Ser Leu Leu Leu Phe Ser Ala Pro Ile Arg Ala  
 85 90 95  
 Thr Ala Tyr Ser Lys Ser Val Trp Asp Leu Gly Trp Phe Val Cys Lys  
 100 105 110  
 Ser Ser Asp Trp Phe Ile His Thr Cys Met Ala Ala Lys Ser Leu Thr  
 115 120 125  
 Ile Val Val Val Ala Lys Val Cys Phe Met Tyr Ala Ser Asp Pro Ala  
 130 135 140  
 Lys Gln Val Ser Ile His Asn Tyr Thr Ile Trp Ser Val Leu Val Ala  
 145 150 155 160  
 Ile Trp Thr Val Ala Ser Leu Leu Pro Leu Pro Glu Trp Phe Phe Ser  
 165 170 175  
 Thr Ile Arg His His Glu Gly Val Glu Met Cys Leu Val Asp Val Pro  
 180 185 190  
 Ala Val Ala Glu Glu Phe Met Ser Met Phe Gly Lys Leu Tyr Pro Leu  
 195 200 205  
 Leu Ala Phe Gly Leu Pro Leu Phe Phe Ala Ser Phe Tyr Phe Trp Arg  
 210 215 220  
 Ala Tyr Asp Gln Cys Lys Lys Arg Gly Thr Lys Thr Gln Asn Leu Arg  
 225 230 235 240  
 Asn Gln Ile Arg Ser Lys Gln Val Thr Val Met Leu Leu Ser Ile Ala

241/518

	245		250		255
Ile Ile Ser Ala Val Leu Trp Leu Pro Glu Trp Val Ala Trp Leu Trp					
	260		265		270
Val Trp His Leu Lys Ala Ala Gly Pro Ala Pro Pro Gln Gly Phe Ile					
	275		280		285
Ala Leu Ser Gln Val Leu Met Phe Ser Ile Ser Ser Ala Asn Pro Leu					
	290		295		300
Ile Phe Leu Val Met Ser Glu Glu Phe Arg Glu Gly Leu Lys Gly Val					
305		310		315	320
Trp Lys Trp Met Ile Thr Lys Lys Pro Pro Thr Val Ser Glu Ser Gln					
	325		330		335
Glu Thr Pro Ala Gly Asn Ser Glu Gly Leu Pro Asp Lys Val Pro Ser					
	340		345		350
Pro Glu Ser Pro Ala Ser Ile Pro Glu Lys Glu Lys Pro Ser Ser Pro					
	355		360		365
Ser Ser Gly Lys Gly Lys Thr Glu Lys Ala Glu Ile Pro Ile Leu Pro					
	370		375		380
Asp Val Glu Gln Phe Trp His Glu Arg Asp Thr Val Pro Ser Val Gln					
385		390		395	400
Asp Asn Asp Pro Ile Pro Trp Glu His Glu Asp Gln Glu Thr Gly Glu					
	405		410		415
Gly Val Lys Thr Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro					
	420		425		430
Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val					
	435		440		445
Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys					
	450		455		460
Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val					
465		470		475	480

242/518

Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His  
 485 490 495  
 Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val  
 500 505 510  
 Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg  
 515 520 525  
 Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu  
 530 535 540  
 Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu  
 545 550 555 560  
 Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln  
 565 570 575  
 Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp  
 580 585 590  
 Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly  
 595 600 605  
 Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser  
 610 615 620  
 Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu  
 625 630 635 640  
 Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr  
 645 650 655

Asn

&lt;210&gt; 97

&lt;211&gt; 1232

&lt;212&gt; PRT

&lt;213&gt; Human

243/518

&lt;400&gt; 97

Met Val Cys Ser Ala Ala Pro Leu Leu Leu Leu Ala Thr Thr Leu Pro  
                     5                    10                    15  
 Leu Leu Gly Ser Pro Val Ala Gln Ala Ser Gln Pro Gly Gln Ser Gln  
                     20                    25                    30  
 Ala Gly Gly Glu Ser Gly Ser Gly Gln Leu Leu Asp Gln Glu Asn Gly  
                     35                    40                    45  
 Ala Gly Glu Ser Ala Leu Val Ser Val Tyr Val His Leu Asp Phe Pro  
                     50                    55                    60  
 Asp Lys Thr Trp Pro Pro Glu Leu Ser Arg Thr Leu Thr Leu Pro Ala  
                     65                    70                    75                    80  
 Ala Ser Ala Ser Ser Ser Pro Arg Pro Leu Leu Thr Gly Leu Arg Leu  
                     85                    90                    95  
 Thr Thr Glu Cys Asn Val Asn His Lys Gly Asn Phe Tyr Cys Ala Cys  
                     100                    105                    110  
 Leu Ser Gly Tyr Gln Trp Asn Thr Ser Ile Cys Leu His Tyr Pro Pro  
                     115                    120                    125  
 Cys Gln Ser Leu His Asn His Gln Pro Cys Gly Cys Leu Val Phe Ser  
                     130                    135                    140  
 His Pro Glu Pro Gly Tyr Cys Gln Leu Leu Pro Pro Val Pro Gly Ile  
                     145                    150                    155                    160  
 Leu Asn Leu Asn Ser Gln Leu Gln Met Pro Gly Asp Thr Leu Ser Leu  
                     165                    170                    175  
 Thr Leu His Leu Ser Gln Glu Ala Thr Asn Leu Ser Trp Phe Leu Arg  
                     180                    185                    190  
 His Pro Gly Ser Pro Ser Pro Ile Leu Leu Gln Pro Gly Thr Gln Val  
                     195                    200                    205  
 Ser Val Thr Ser Ser His Gly Gln Ala Ala Leu Ser Val Ser Asn Met  
                     210                    215                    220



244/518

Ser His His Trp Ala Gly Glu Tyr Met Ser Cys Phe Glu Ala Gln Gly  
 225                      230                      235                      240  
 Phe Lys Trp Asn Leu Tyr Glu Val Val Arg Val Pro Leu Lys Ala Thr  
                          245                      250                      255  
 Asp Val Ala Arg Leu Pro Tyr Gln Leu Ser Ile Ser Cys Ala Thr Ser  
                          260                      265                      270  
 Pro Gly Phe Gln Leu Ser Cys Cys Ile Pro Ser Thr Asn Leu Ala Tyr  
                          275                      280                      285  
 Thr Ala Ala Trp Ser Pro Gly Glu Gly Ser Lys Ala Ser Ser Phe Asn  
                          290                      295                      300  
 Glu Ser Gly Ser Gln Cys Phe Val Leu Ala Val Gln Arg Cys Pro Met  
 305                      310                      315                      320  
 Ala Asp Thr Thr Tyr Thr Cys Asp Leu Gln Ser Leu Gly Leu Ala Pro  
                          325                      330                      335  
 Leu Arg Val Pro Ile Ser Ile Thr Ile Ile Gln Asp Gly Asp Ile Thr  
                          340                      345                      350  
 Cys Pro Glu Asp Ala Ser Val Leu Thr Trp Asn Val Thr Lys Ala Gly  
                          355                      360                      365  
 His Val Ala Gln Ala Pro Cys Pro Glu Ser Lys Arg Gly Ile Val Arg  
                          370                      375                      380  
 Arg Leu Cys Gly Ala Asp Gly Val Trp Gly Pro Val His Ser Ser Cys  
 385                      390                      395                      400  
 Thr Asp Ala Arg Leu Leu Ala Leu Phe Thr Arg Thr Lys Leu Leu Gln  
                          405                      410                      415  
 Ala Gly Gln Gly Ser Pro Ala Glu Glu Val Pro Gln Ile Leu Ala Gln  
                          420                      425                      430  
 Leu Pro Gly Gln Ala Ala Glu Ala Ser Ser Pro Ser Asp Leu Leu Thr  
                          435                      440                      445  
 Leu Leu Ser Thr Met Lys Tyr Val Ala Lys Val Val Ala Glu Ala Arg

245/518

450	455	460	
Ile Gln Leu Asp Arg Arg Ala Leu Lys Asn Leu Leu Ile Ala Thr Asp			
465	470	475	480
Lys Val Leu Asp Met Asp Thr Arg Ser Leu Trp Thr Leu Ala Gln Ala			
485	490	495	
Arg Lys Pro Trp Ala Gly Ser Thr Leu Leu Leu Ala Val Glu Thr Leu			
500	505	510	
Ala Cys Ser Leu Cys Pro Gln Asp Tyr Pro Phe Ala Phe Ser Leu Pro			
515	520	525	
Asn Val Leu Leu Gln Ser Gln Leu Phe Gly Pro Thr Phe Pro Ala Asp			
530	535	540	
Tyr Ser Ile Ser Phe Pro Thr Arg Pro Pro Leu Gln Ala Gln Ile Pro			
545	550	555	560
Arg His Ser Leu Ala Pro Leu Val Arg Asn Gly Thr Glu Ile Ser Ile			
565	570	575	
Thr Ser Leu Val Leu Arg Lys Leu Asp His Leu Leu Pro Ser Asn Tyr			
580	585	590	
Gly Gln Gly Leu Gly Asp Ser Leu Tyr Ala Thr Pro Gly Leu Val Leu			
595	600	605	
Val Ile Ser Ile Met Ala Gly Asp Arg Ala Phe Ser Gln Gly Glu Val			
610	615	620	
Ile Met Asp Phe Gly Asn Thr Asp Gly Ser Pro His Cys Val Phe Trp			
625	630	635	640
Asp His Ser Leu Phe Gln Gly Arg Gly Gly Trp Ser Lys Glu Gly Cys			
645	650	655	
Gln Ala Gln Val Ala Ser Ala Ser Pro Thr Ala Gln Cys Leu Cys Gln			
660	665	670	
His Leu Thr Ala Phe Ser Val Leu Met Ser Pro His Thr Val Pro Glu			
675	680	685	

246/518

Glu Pro Ala Leu Ala Leu Leu Thr Gln Val Gly Leu Gly Ala Ser Ile  
 690 695 700  
 Leu Ala Leu Leu Val Cys Leu Gly Val Tyr Trp Leu Val Trp Arg Val  
 705 710 715 720  
 Val Val Arg Asn Lys Ile Ser Tyr Phe Arg His Ala Ala Leu Leu Asn  
 725 730 735  
 Met Val Phe Cys Leu Leu Ala Ala Asp Thr Cys Phe Leu Gly Ala Pro  
 740 745 750  
 Phe Leu Ser Pro Gly Pro Arg Ser Pro Leu Cys Leu Ala Ala Ala Phe  
 755 760 765  
 Leu Cys His Phe Leu Tyr Leu Ala Thr Phe Phe Trp Met Leu Ala Gln  
 770 775 780  
 Ala Leu Val Leu Ala His Gln Leu Leu Phe Val Phe His Gln Leu Ala  
 785 790 795 800  
 Lys His Arg Val Leu Pro Leu Met Val Leu Leu Gly Tyr Leu Cys Pro  
 805 810 815  
 Leu Gly Leu Ala Gly Val Thr Leu Gly Leu Tyr Leu Pro Gln Gly Gln  
 820 825 830  
 Tyr Leu Arg Glu Gly Glu Cys Trp Leu Asp Gly Lys Gly Gly Ala Leu  
 835 840 845  
 Tyr Thr Phe Val Gly Pro Val Leu Ala Ile Ile Gly Val Asn Gly Leu  
 850 855 860  
 Val Leu Ala Met Ala Met Leu Lys Leu Leu Arg Pro Ser Leu Ser Glu  
 865 870 875 880  
 Gly Pro Pro Ala Glu Lys Arg Gln Ala Leu Leu Gly Val Ile Lys Ala  
 885 890 895  
 Leu Leu Ile Leu Thr Pro Ile Phe Gly Leu Thr Trp Gly Leu Gly Leu  
 900 905 910  
 Ala Thr Leu Leu Glu Glu Val Ser Thr Val Pro His Tyr Ile Phe Thr

247/518

915	920	925
Ile Leu Asn Thr Leu Gln Gly Val Phe Ile Leu Leu Phe Gly Cys Leu		
930	935	940
Met Asp Arg Lys Ile Gln Glu Ala Leu Arg Lys Arg Phe Cys Arg Ala		
945	950	955
Gln Ala Pro Ser Ser Thr Ile Ser Leu Ala Thr Asn Glu Gly Cys Ile		
965	970	975
Leu Glu His Ser Lys Gly Gly Ser Asp Thr Ala Arg Lys Thr Asp Ala		
980	985	990
Ser Glu Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile		
995	1000	1005
Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser		
1010	1015	1020
Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe		
1025	1030	1035
Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr		
1045	1050	1055
Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met		
1060	1065	1070
Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln		
1075	1080	1085
Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala		
1090	1095	1100
Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys		
1105	1110	1115
Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu		
1125	1130	1135
Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys		
1140	1145	1150

248/518

Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly

1155

1160

1165

Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp

1170

1175

1180

Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala

1185

1190

1195

1200

Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu

1205

1210

1215

Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn

1220

1225

1230

&lt;210&gt; 98

&lt;211&gt; 931

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 98

Met Thr Pro Gln Ser Leu Leu Gln Thr Thr Leu Phe Leu Leu Ser Leu

5

10

15

Leu Phe Leu Val Gln Gly Ala His Gly Arg Gly His Arg Glu Asp Phe

20

25

30

Arg Phe Cys Ser Gln Arg Asn Gln Thr His Arg Ser Ser Leu His Tyr

35

40

45

Lys Pro Thr Pro Asp Leu Arg Ile Ser Ile Glu Asn Ser Glu Glu Ala

50

55

60

Leu Thr Val His Ala Pro Phe Pro Ala Ala His Pro Ala Ser Arg Ser

65

70

75

80

Phe Pro Asp Pro Arg Gly Leu Tyr His Phe Cys Leu Tyr Trp Asn Arg

85

90

95

249/518

His Ala Gly Arg Leu His Leu Leu Tyr Gly Lys Arg Asp Phe Leu Leu  
 100 105 110  
 Ser Asp Lys Ala Ser Ser Leu Leu Cys Phe Gln His Gln Glu Glu Ser  
 115 120 125  
 Leu Ala Gln Gly Pro Pro Leu Leu Ala Thr Ser Val Thr Ser Trp Trp  
 130 135 140  
 Ser Pro Gln Asn Ile Ser Leu Pro Ser Ala Ala Ser Phe Thr Phe Ser  
 145 150 155 160  
 Phe His Ser Pro Pro His Thr Ala Ala His Asn Ala Ser Val Asp Met  
 165 170 175  
 Cys Glu Leu Lys Arg Asp Leu Gln Leu Leu Ser Gln Phe Leu Lys His  
 180 185 190  
 Pro Gln Lys Ala Ser Arg Arg Pro Ser Ala Ala Pro Ala Ser Gln Gln  
 195 200 205  
 Leu Gln Ser Leu Glu Ser Lys Leu Thr Ser Val Arg Phe Met Gly Asp  
 210 215 220  
 Met Val Ser Phe Glu Glu Asp Arg Ile Asn Ala Thr Val Trp Lys Leu  
 225 230 235 240  
 Gln Pro Thr Ala Gly Leu Gln Asp Leu His Ile His Ser Arg Gln Glu  
 245 250 255  
 Glu Glu Gln Ser Glu Ile Met Glu Tyr Ser Val Leu Leu Pro Arg Thr  
 260 265 270  
 Leu Phe Gln Arg Thr Lys Gly Arg Ser Gly Glu Ala Glu Lys Arg Leu  
 275 280 285  
 Leu Leu Val Asp Phe Ser Ser Gln Ala Leu Phe Gln Asp Lys Asn Ser  
 290 295 300  
 Ser Gln Val Leu Gly Glu Lys Val Leu Gly Ile Val Val Gln Asn Thr  
 305 310 315 320  
 Lys Val Ala Asn Leu Thr Glu Pro Val Val Leu Thr Phe Gln His Gln

250/518

325	330	335
Leu Gln Pro Lys Asn Val Thr Leu Gln Cys Val Phe Trp Val Glu Asp		
340	345	350
Pro Thr Leu Ser Ser Pro Gly His Trp Ser Ser Ala Gly Cys Glu Thr		
355	360	365
Val Arg Arg Glu Thr Gln Thr Ser Cys Phe Cys Asn His Leu Thr Tyr		
370	375	380
Phe Ala Val Leu Met Val Ser Ser Val Glu Val Asp Ala Val His Lys		
385	390	395
His Tyr Leu Ser Leu Leu Ser Tyr Val Gly Cys Val Val Ser Ala Leu		
405	410	415
Ala Cys Leu Val Thr Ile Ala Ala Tyr Leu Cys Ser Arg Val Pro Leu		
420	425	430
Pro Cys Arg Arg Lys Pro Arg Asp Tyr Thr Ile Lys Val His Met Asn		
435	440	445
Leu Leu Leu Ala Val Phe Leu Leu Asp Thr Ser Phe Leu Leu Ser Glu		
450	455	460
Pro Val Ala Leu Thr Gly Ser Glu Ala Gly Cys Arg Ala Ser Ala Ile		
465	470	475
Phe Leu His Phe Ser Leu Leu Thr Cys Leu Ser Trp Met Gly Leu Glu		
485	490	495
Gly Tyr Asn Leu Tyr Arg Leu Val Val Glu Val Phe Gly Thr Tyr Val		
500	505	510
Pro Gly Tyr Leu Leu Lys Leu Ser Ala Met Gly Trp Gly Phe Pro Ile		
515	520	525
Phe Leu Val Thr Leu Val Ala Leu Val Asp Val Asp Asn Tyr Gly Pro		
530	535	540
Ile Ile Leu Ala Val His Arg Thr Pro Glu Gly Val Ile Tyr Pro Ser		
545	550	555
		560

251/518

Met Cys Trp Ile Arg Asp Ser Leu Val Ser Tyr Ile Thr Asn Leu Gly			
	565	570	575
Leu Phe Ser Leu Val Phe Leu Phe Asn Met Ala Met Leu Ala Thr Met			
	580	585	590
Val Val Gln Ile Leu Arg Leu Arg Pro His Thr Gln Lys Trp Ser His			
	595	600	605
Val Leu Thr Leu Leu Gly Leu Ser Leu Val Leu Gly Leu Pro Trp Ala			
	610	615	620
Leu Ile Phe Phe Ser Phe Ala Ser Gly Thr Phe Gln Leu Val Val Leu			
625	630	635	640
Tyr Leu Phe Ser Ile Ile Thr Ser Phe Gln Gly Phe Leu Ile Phe Ile			
	645	650	655
Trp Tyr Trp Ser Met Arg Leu Gln Ala Arg Gly Gly Pro Ser Pro Leu			
	660	665	670
Lys Ser Asn Ser Asp Ser Ala Arg Leu Pro Ile Ser Ser Gly Ser Thr			
	675	680	685
Ser Ser Ser Arg Ile Ser Ser Lys Gly Glu Glu Leu Phe Thr Gly Val			
	690	695	700
Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe			
705	710	715	720
Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr			
	725	730	735
Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr			
	740	745	750
Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro			
	755	760	765
Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly			
	770	775	780
Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys			



252/518

785	790	795	800
Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile			
805	810	815	
Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His			
820	825	830	
Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp			
835	840	845	
Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile			
850	855	860	
Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro			
865	870	875	880
Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr			
885	890	895	
Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val			
900	905	910	
Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu			
915	920	925	
Leu Tyr Asn			
930			

&lt;210&gt; 99

&lt;211&gt; 1584

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 99

Met Lys Ser Pro Arg Arg Thr Thr Leu Cys Leu Met Phe Ile Val Ile		
5	10	15
Tyr Ser Ser Lys Ala Ala Leu Asn Trp Asn Tyr Glu Ser Thr Ile His		

				20						25					30				
Pro	Leu	Ser	Leu	His	Glu	His	Glu	Pro	Ala	Gly	Glu	Glu	Ala	Leu	Arg				
		35						40					45						
Gln	Lys	Arg	Ala	Val	Ala	Thr	Lys	Ser	Pro	Thr	Ala	Glu	Glu	Tyr	Thr				
	50						55					60							
Val	Asn	Ile	Glu	Ile	Ser	Phe	Glu	Asn	Ala	Ser	Phe	Leu	Asp	Pro	Ile				
65						70					75				80				
Lys	Ala	Tyr	Leu	Asn	Ser	Leu	Ser	Phe	Pro	Ile	His	Gly	Asn	Asn	Thr				
				85					90						95				
Asp	Gln	Ile	Thr	Asp	Ile	Leu	Ser	Ile	Asn	Val	Thr	Thr	Val	Cys	Arg				
			100					105					110						
Pro	Ala	Gly	Asn	Glu	Ile	Trp	Cys	Ser	Cys	Glu	Thr	Gly	Tyr	Gly	Trp				
		115						120					125						
Pro	Arg	Glu	Arg	Cys	Leu	His	Asn	Leu	Ile	Cys	Gln	Glu	Arg	Asp	Val				
	130						135					140							
Phe	Leu	Pro	Gly	His	His	Cys	Ser	Cys	Leu	Lys	Glu	Leu	Pro	Pro	Asn				
145						150				155					160				
Gly	Pro	Phe	Cys	Leu	Leu	Gln	Glu	Asp	Val	Thr	Leu	Asn	Met	Arg	Val				
				165					170						175				
Arg	Leu	Asn	Val	Gly	Phe	Gln	Glu	Asp	Leu	Met	Asn	Thr	Ser	Ser	Ala				
			180					185					190						
Leu	Tyr	Arg	Ser	Tyr	Lys	Thr	Asp	Leu	Glu	Thr	Ala	Phe	Arg	Lys	Gly				
		195						200					205						
Tyr	Gly	Ile	Leu	Pro	Gly	Phe	Lys	Gly	Val	Thr	Val	Thr	Gly	Phe	Lys				
	210						215						220						
Ser	Gly	Ser	Val	Val	Val	Thr	Tyr	Glu	Val	Lys	Thr	Thr	Pro	Pro	Ser				
225						230				235					240				
Leu	Glu	Leu	Ile	His	Lys	Ala	Asn	Glu	Gln	Val	Val	Gln	Ser	Leu	Asn				
				245					250						255				

254/518

Gln Thr Tyr Lys Met Asp Tyr Asn Ser Phe Gln Ala Val Thr Ile Asn  
 260 265 270  
 Glu Ser Asn Phe Phe Val Thr Pro Glu Ile Ile Phe Glu Gly Asp Thr  
 275 280 285  
 Val Ser Leu Val Cys Glu Lys Glu Val Leu Ser Ser Asn Val Ser Trp  
 290 295 300  
 Arg Tyr Glu Glu Gln Gln Leu Glu Ile Gln Asn Ser Ser Arg Phe Ser  
 305 310 315 320  
 Ile Tyr Thr Ala Leu Phe Asn Asn Met Thr Ser Val Ser Lys Leu Thr  
 325 330 335  
 Ile His Asn Ile Thr Pro Gly Asp Ala Gly Glu Tyr Val Cys Lys Leu  
 340 345 350  
 Ile Leu Asp Ile Phe Glu Tyr Glu Cys Lys Lys Lys Ile Asp Val Met  
 355 360 365  
 Pro Ile Gln Ile Leu Ala Asn Glu Glu Met Lys Val Met Cys Asp Asn  
 370 375 380  
 Asn Pro Val Ser Leu Asn Cys Cys Ser Gln Gly Asn Val Asn Trp Ser  
 385 390 395 400  
 Lys Val Glu Trp Lys Gln Glu Gly Lys Ile Asn Ile Pro Gly Thr Pro  
 405 410 415  
 Glu Thr Asp Ile Asp Ser Ser Cys Ser Arg Tyr Thr Leu Lys Ala Asp  
 420 425 430  
 Gly Thr Gln Cys Pro Ser Gly Ser Ser Gly Thr Thr Val Ile Tyr Thr  
 435 440 445  
 Cys Glu Phe Ile Ser Ala Tyr Gly Ala Arg Gly Ser Ala Asn Ile Lys  
 450 455 460  
 Val Thr Phe Ile Ser Val Ala Asn Leu Thr Ile Thr Pro Asp Pro Ile  
 465 470 475 480  
 Ser Val Ser Glu Gly Gln Asn Phe Ser Ile Lys Cys Ile Ser Asp Val

255/518

485	490	495
Ser Asn Tyr Asp Glu Val Tyr Trp Asn Thr Ser Ala Gly Ile Lys Ile		
500	505	510
Tyr Gln Arg Phe Tyr Thr Thr Arg Arg Tyr Leu Asp Gly Ala Glu Ser		
515	520	525
Val Leu Thr Val Lys Thr Ser Thr Arg Glu Trp Asn Gly Thr Tyr His		
530	535	540
Cys Ile Phe Arg Tyr Lys Asn Ser Tyr Ser Ile Ala Thr Lys Asp Val		
545	550	555
Ile Val His Pro Leu Pro Leu Lys Leu Asn Ile Met Val Asp Pro Leu		
565	570	575
Glu Ala Thr Val Ser Cys Ser Gly Ser His His Ile Lys Cys Cys Ile		
580	585	590
Glu Glu Asp Gly Asp Tyr Lys Val Thr Phe His Met Gly Ser Ser Ser		
595	600	605
Leu Pro Ala Ala Lys Glu Val Asn Lys Lys Gln Val Cys Tyr Lys His		
610	615	620
Asn Phe Asn Ala Ser Ser Val Ser Trp Cys Ser Lys Thr Val Asp Val		
625	630	635
Cys Cys His Phe Thr Asn Ala Ala Asn Asn Ser Val Trp Ser Pro Ser		
645	650	655
Met Lys Leu Asn Leu Val Pro Gly Glu Asn Ile Thr Cys Gln Asp Pro		
660	665	670
Val Ile Gly Val Gly Glu Pro Gly Lys Val Ile Gln Lys Leu Cys Arg		
675	680	685
Phe Ser Asn Val Pro Ser Ser Pro Glu Ser Pro Ile Gly Gly Thr Ile		
690	695	700
Thr Tyr Lys Cys Val Gly Ser Gln Trp Glu Glu Lys Arg Asn Asp Cys		
705	710	715
		720

256/518

Ile Ser Ala Pro Ile Asn Ser Leu Leu Gln Met Ala Lys Ala Leu Ile  
                     725                    730                    735  
 Lys Ser Pro Ser Gln Asp Glu Met Leu Pro Thr Tyr Leu Lys Asp Leu  
                     740                    745                    750  
 Ser Ile Ser Ile Asp Lys Ala Glu His Glu Ile Ser Ser Ser Pro Gly  
                     755                    760                    765  
 Ser Leu Gly Ala Ile Ile Asn Ile Leu Asp Leu Leu Ser Thr Val Pro  
                     770                    775                    780  
 Thr Gln Val Asn Ser Glu Met Met Thr His Val Leu Ser Thr Val Asn  
 785                    790                    795                    800  
 Val Ile Leu Gly Lys Pro Val Leu Asn Thr Trp Lys Val Leu Gln Gln  
                     805                    810                    815  
 Gln Trp Thr Asn Gln Ser Ser Gln Leu Leu His Ser Val Glu Arg Phe  
                     820                    825                    830  
 Ser Gln Ala Leu Gln Ser Gly Asp Ser Pro Pro Leu Ser Phe Ser Gln  
                     835                    840                    845  
 Thr Asn Val Gln Met Ser Ser Thr Val Ile Lys Ser Ser His Pro Glu  
                     850                    855                    860  
 Thr Tyr Gln Gln Arg Phe Val Phe Pro Tyr Phe Asp Leu Trp Gly Asn  
 865                    870                    875                    880  
 Val Val Ile Asp Lys Ser Tyr Leu Glu Asn Leu Gln Ser Asp Ser Ser  
                     885                    890                    895  
 Ile Val Thr Met Ala Phe Pro Thr Leu Gln Ala Ile Leu Ala Gln Asp  
                     900                    905                    910  
 Ile Gln Glu Asn Asn Phe Ala Glu Ser Leu Val Met Thr Thr Thr Val  
                     915                    920                    925  
 Ser His Asn Thr Thr Met Pro Phe Arg Ile Ser Met Thr Phe Lys Asn  
                     930                    935                    940  
 Asn Ser Pro Ser Gly Gly Glu Thr Lys Cys Val Phe Trp Asn Phe Arg

257/518

945	950	955	960
Leu Ala Asn Asn Thr Gly Gly Trp Asp Ser Ser Gly Cys Tyr Val Glu			
	965	970	975
Glu Gly Asp Gly Asp Asn Val Thr Cys Ile Cys Asp His Leu Thr Ser			
	980	985	990
Phe Ser Ile Leu Met Ser Pro Asp Ser Pro Asp Pro Ser Ser Leu Leu			
	995	1000	1005
Gly Ile Leu Leu Asp Ile Ile Ser Tyr Val Gly Val Gly Phe Ser Ile			
	1010	1015	1020
Leu Ser Leu Ala Ala Cys Leu Val Val Glu Ala Val Val Trp Lys Ser			
	1025	1030	1035
Val Thr Lys Asn Arg Thr Ser Tyr Met Arg His Thr Cys Ile Val Asn			
	1045	1050	1055
Ile Ala Ala Ser Leu Leu Val Ala Asn Thr Trp Phe Ile Val Val Ala			
	1060	1065	1070
Ala Ile Gln Asp Asn Arg Tyr Ile Leu Cys Lys Thr Ala Cys Val Ala			
	1075	1080	1085
Ala Thr Phe Phe Ile His Phe Phe Tyr Leu Ser Val Phe Phe Trp Met			
	1090	1095	1100
Leu Thr Leu Gly Leu Met Leu Phe Tyr Arg Leu Val Phe Ile Leu His			
	1105	1110	1115
Glu Thr Ser Arg Ser Thr Gln Lys Ala Ile Ala Phe Cys Leu Gly Tyr			
	1125	1130	1135
Gly Cys Pro Leu Ala Ile Ser Val Ile Thr Leu Gly Ala Thr Gln Pro			
	1140	1145	1150
Arg Glu Val Tyr Thr Arg Lys Asn Val Cys Trp Leu Asn Trp Glu Asp			
	1155	1160	1165
Thr Lys Ala Leu Leu Ala Phe Ala Ile Pro Ala Leu Ile Ile Val Val			
	1170	1175	1180

258/518

Val Asn Ile Thr Ile Thr Ile Val Val Ile Thr Lys Ile Leu Arg Pro			
1185	1190	1195	1200
Ser Ile Gly Asp Lys Pro Cys Lys Gln Glu Lys Ser Ser Leu Phe Gln			
	1205	1210	1215
Ile Ser Lys Ser Ile Gly Val Leu Thr Pro Leu Leu Gly Leu Thr Trp			
	1220	1225	1230
Gly Phe Gly Leu Thr Thr Val Phe Pro Gly Thr Asn Leu Val Phe His			
	1235	1240	1245
Ile Ile Phe Ala Ile Leu Asn Val Phe Gln Gly Leu Phe Ile Leu Leu			
	1250	1255	1260
Phe Gly Cys Leu Trp Asp Leu Lys Val Gln Glu Ala Leu Leu Asn Lys			
1265	1270	1275	1280
Phe Ser Leu Ser Arg Trp Ser Ser Gln His Ser Lys Ser Thr Ser Leu			
	1285	1290	1295
Gly Ser Ser Thr Pro Val Phe Ser Met Ser Ser Pro Ile Ser Arg Arg			
	1300	1305	1310
Phe Asn Asn Leu Phe Gly Lys Thr Gly Thr Tyr Asn Val Ser Thr Pro			
	1315	1320	1325
Glu Ala Thr Ser Ser Ser Leu Glu Asn Ser Ser Ser Ala Ser Ser Leu			
	1330	1335	1340
Leu Asn Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile			
1345	1350	1355	1360
Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser			
	1365	1370	1375
Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe			
	1380	1385	1390
Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr			
	1395	1400	1405
Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met			

259/518

1410                      1415                      1420  
 Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln  
 1425                      1430                      1435                      1440  
 Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala  
                     1445                      1450                      1455  
 Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys  
                     1460                      1465                      1470  
 Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu  
                     1475                      1480                      1485  
 Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys  
                     1490                      1495                      1500  
 Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly  
 1505                      1510                      1515                      1520  
 Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp  
                     1525                      1530                      1535  
 Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala  
                     1540                      1545                      1550  
 Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu  
                     1555                      1560                      1565  
 Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
                     1570                      1575                      1580

&lt;210&gt; 100

&lt;211&gt; 645

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 100

Met Ser Leu Asn Ser Ser Leu Ser Cys Arg Lys Glu Leu Ser Asn Leu



				5						10					15				
Thr	Glu	Glu	Glu	Gly	Gly	Glu	Gly	Gly	Val	Ile	Ile	Thr	Gln	Phe	Ile				
				20					25					30					
Ala	Ile	Ile	Val	Ile	Thr	Ile	Phe	Val	Cys	Leu	Gly	Asn	Leu	Val	Ile				
				35				40					45						
Val	Val	Thr	Leu	Tyr	Lys	Lys	Ser	Tyr	Leu	Leu	Thr	Leu	Ser	Asn	Lys				
				50			55					60							
Phe	Val	Phe	Ser	Leu	Thr	Leu	Ser	Asn	Phe	Leu	Leu	Ser	Val	Leu	Val				
				65			70				75				80				
Leu	Pro	Phe	Val	Val	Thr	Ser	Ser	Ile	Arg	Arg	Glu	Trp	Ile	Phe	Gly				
				85					90					95					
Val	Val	Trp	Cys	Asn	Phe	Ser	Ala	Leu	Leu	Tyr	Leu	Leu	Ile	Ser	Ser				
				100					105				110						
Ala	Ser	Met	Leu	Thr	Leu	Gly	Val	Ile	Ala	Ile	Asp	Arg	Tyr	Tyr	Ala				
				115				120					125						
Val	Leu	Tyr	Pro	Met	Val	Tyr	Pro	Met	Lys	Ile	Thr	Gly	Asn	Arg	Ala				
				130				135				140							
Val	Met	Ala	Leu	Val	Tyr	Ile	Trp	Leu	His	Ser	Leu	Ile	Gly	Cys	Leu				
				145			150				155				160				
Pro	Pro	Leu	Phe	Gly	Trp	Ser	Ser	Val	Glu	Phe	Asp	Glu	Phe	Lys	Trp				
				165					170					175					
Met	Cys	Val	Ala	Ala	Trp	His	Arg	Glu	Pro	Gly	Tyr	Thr	Ala	Phe	Trp				
				180					185				190						
Gln	Ile	Trp	Cys	Ala	Leu	Phe	Pro	Phe	Leu	Val	Met	Leu	Val	Cys	Tyr				
				195				200				205							
Gly	Phe	Ile	Phe	Arg	Val	Ala	Arg	Val	Lys	Ala	Arg	Lys	Val	His	Cys				
				210			215				220								
Gly	Thr	Val	Val	Ile	Val	Glu	Glu	Asp	Ala	Gln	Arg	Thr	Gly	Arg	Lys				
				225			230				235				240				

261/518

Asn Ser Ser Thr Ser Thr Ser Ser Ser Gly Ser Arg Arg Asn Ala Phe  
                   245                  250                  255  
 Gln Gly Val Val Tyr Ser Ala Asn Gln Cys Lys Ala Leu Ile Thr Ile  
                   260                  265                  270  
 Leu Val Val Leu Gly Ala Phe Met Val Thr Trp Gly Pro Tyr Met Val  
                   275                  280                  285  
 Val Ile Ala Ser Glu Ala Leu Trp Gly Lys Ser Ser Val Ser Pro Ser  
                   290                  295                  300  
 Leu Glu Thr Trp Ala Thr Trp Leu Ser Phe Ala Ser Ala Val Cys His  
 305                  310                  315                  320  
 Pro Leu Ile Tyr Gly Leu Trp Asn Lys Thr Val Arg Lys Glu Leu Leu  
                   325                  330                  335  
 Gly Met Cys Phe Gly Asp Arg Tyr Tyr Arg Glu Pro Phe Val Gln Arg  
                   340                  345                  350  
 Gln Arg Thr Ser Arg Leu Phe Ser Ile Ser Asn Arg Ile Thr Asp Leu  
                   355                  360                  365  
 Gly Leu Ser Pro His Leu Thr Ala Leu Met Ala Gly Gly Gln Pro Leu  
                   370                  375                  380  
 Gly His Ser Ser Ser Thr Gly Asp Thr Gly Phe Ser Cys Ser Gln Asp  
 385                  390                  395                  400  
 Ser Gly Asn Leu Arg Ala Leu Ala Ser Lys Gly Glu Glu Leu Phe Thr  
                   405                  410                  415  
 Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His  
                   420                  425                  430  
 Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys  
                   435                  440                  445  
 Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp  
                   450                  455                  460  
 Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg

262/518

465                      470                      475                      480  
 Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro  
                          485                      490                      495  
 Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn  
                          500                      505                      510  
 Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn  
                          515                      520                      525  
 Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu  
                          530                      535                      540  
 Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met  
 545                      550                      555                      560  
 Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His  
                          565                      570                      575  
 Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn  
                          580                      585                      590  
 Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu  
                          595                      600                      605  
 Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His  
                          610                      615                      620  
 Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met  
 625                      630                      635                      640  
 Asp Glu Leu Tyr Asn  
                          645

&lt;210&gt; 101

&lt;211&gt; 637

&lt;212&gt; PRT

&lt;213&gt; Human

263/518

&lt;400&gt; 101

Met	Ala	Gln	Arg	Ala	Phe	Pro	Asn	Pro	Tyr	Ala	Asp	Tyr	Asn	Lys	Ser
				5					10					15	
Leu	Ala	Glu	Gly	Tyr	Phe	Asp	Ala	Ala	Gly	Arg	Leu	Thr	Pro	Glu	Phe
				20				25					30		
Ser	Gln	Arg	Leu	Thr	Asn	Lys	Ile	Arg	Glu	Leu	Leu	Gln	Gln	Met	Glu
				35			40					45			
Arg	Gly	Leu	Lys	Ser	Ala	Asp	Pro	Arg	Asp	Gly	Thr	Gly	Tyr	Thr	Gly
				50			55					60			
Trp	Ala	Gly	Ile	Ala	Val	Leu	Tyr	Leu	His	Leu	Tyr	Asp	Val	Phe	Gly
				65			70				75			80	
Asp	Pro	Ala	Tyr	Leu	Gln	Leu	Ala	His	Gly	Tyr	Val	Lys	Gln	Ser	Leu
					85				90				95		
Asn	Cys	Leu	Thr	Lys	Arg	Ser	Ile	Thr	Phe	Leu	Cys	Gly	Asp	Ala	Gly
				100				105					110		
Pro	Leu	Ala	Val	Ala	Ala	Val	Leu	Tyr	His	Lys	Met	Asn	Asn	Glu	Lys
				115			120						125		
Gln	Ala	Glu	Asp	Cys	Ile	Thr	Arg	Leu	Ile	His	Leu	Asn	Lys	Ile	Asp
				130			135					140			
Pro	His	Ala	Pro	Asn	Glu	Met	Leu	Tyr	Gly	Arg	Ile	Gly	Tyr	Ile	Tyr
				145			150				155			160	
Ala	Leu	Leu	Phe	Val	Asn	Lys	Asn	Phe	Gly	Val	Glu	Lys	Ile	Pro	Gln
				165				170					175		
Ser	His	Ile	Gln	Gln	Ile	Cys	Glu	Thr	Ile	Leu	Thr	Ser	Gly	Glu	Asn
				180				185					190		
Leu	Ala	Arg	Lys	Arg	Asn	Phe	Thr	Ala	Lys	Ser	Pro	Leu	Met	Tyr	Glu
				195			200					205			
Trp	Tyr	Gln	Glu	Tyr	Tyr	Val	Gly	Ala	Ala	His	Gly	Leu	Ala	Gly	Ile
				210			215					220			

264/518

Tyr Tyr Tyr Leu Met Gln Pro Ser Leu Gln Val Ser Gln Gly Lys Leu			
225	230	235	240
His Ser Leu Val Lys Pro Ser Val Asp Tyr Val Cys Gln Leu Lys Phe			
	245	250	255
Pro Ser Gly Asn Tyr Pro Pro Cys Ile Gly Asp Asn Arg Asp Leu Leu			
	260	265	270
Val His Trp Cys His Gly Ala Pro Gly Val Ile Tyr Met Leu Ile Gln			
	275	280	285
Ala Tyr Lys Val Phe Arg Glu Glu Lys Tyr Leu Cys Asp Ala Tyr Gln			
	290	295	300
Cys Ala Asp Val Ile Trp Gln Tyr Gly Leu Leu Lys Lys Gly Tyr Gly			
305	310	315	320
Leu Cys His Gly Ser Ala Gly Asn Ala Tyr Ala Phe Leu Thr Leu Tyr			
	325	330	335
Asn Leu Thr Gln Asp Met Lys Tyr Leu Tyr Arg Ala Cys Lys Phe Ala			
	340	345	350
Glu Trp Cys Leu Glu Tyr Gly Glu His Gly Cys Arg Thr Pro Asp Thr			
	355	360	365
Pro Phe Ser Leu Phe Glu Gly Met Ala Gly Thr Ile Tyr Phe Leu Ala			
	370	375	380
Asp Leu Leu Val Pro Thr Lys Ala Arg Phe Pro Ala Phe Glu Leu Ala			
385	390	395	400
Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu			
	405	410	415
Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly			
	420	425	430
Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr			
	435	440	445
Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys			

265/518

450	455	460
Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His		
465	470	475
Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr		480
	485	490
		495
Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys		
	500	505
		510
Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp		
	515	520
		525
Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr		
	530	535
		540
Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile		
545	550	555
		560
Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln		
	565	570
		575
Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val		
	580	585
		590
Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys		
	595	600
		605
Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr		
	610	615
		620
Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn		
625	630	635

&lt;210&gt; 102

&lt;211&gt; 613

&lt;212&gt; PRT

&lt;213&gt; Human

266/518

&lt;400&gt; 102

Met Ala Asn Ala Ser Glu Pro Gly Gly Ser Gly Gly Gly Glu Ala Ala  
                     5                    10                    15  
 Ala Leu Gly Leu Lys Leu Ala Thr Leu Ser Leu Leu Leu Cys Val Ser  
                     20                    25                    30  
 Leu Ala Gly Asn Val Leu Phe Ala Leu Leu Ile Val Arg Glu Arg Ser  
                     35                    40                    45  
 Leu His Arg Ala Pro Tyr Tyr Leu Leu Leu Asp Leu Cys Leu Ala Asp  
                     50                    55                    60  
 Gly Leu Arg Ala Leu Ala Cys Leu Pro Ala Val Met Leu Ala Ala Arg  
                     65                    70                    75                    80  
 Arg Ala Ala Ala Ala Ala Gly Ala Pro Pro Gly Ala Leu Gly Cys Lys  
                     85                    90                    95  
 Leu Leu Ala Phe Leu Ala Ala Leu Phe Cys Phe His Ala Ala Phe Leu  
                     100                    105                    110  
 Leu Leu Gly Val Gly Val Thr Arg Tyr Leu Ala Ile Ala His His Arg  
                     115                    120                    125  
 Phe Tyr Ala Glu Arg Leu Ala Gly Trp Pro Cys Ala Ala Met Leu Val  
                     130                    135                    140  
 Cys Ala Ala Trp Ala Leu Ala Leu Ala Ala Ala Phe Pro Pro Val Leu  
                     145                    150                    155                    160  
 Asp Gly Gly Gly Asp Asp Glu Asp Ala Pro Cys Ala Leu Glu Gln Arg  
                     165                    170                    175  
 Pro Asp Gly Ala Pro Gly Ala Leu Gly Phe Leu Leu Leu Leu Ala Val  
                     180                    185                    190  
 Val Val Gly Ala Thr His Leu Val Tyr Leu Arg Leu Leu Phe Phe Ile  
                     195                    200                    205  
 His Asp Arg Arg Lys Met Arg Pro Ala Arg Leu Val Pro Ala Val Ser  
                     210                    215                    220

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His Asp Trp Thr Phe His Gly Pro Gly Ala Thr Gly Gln Ala Ala Ala  
 225                      230                      235                      240  
 Asn Trp Thr Ala Gly Phe Gly Arg Gly Pro Thr Pro Pro Ala Leu Val  
                          245                      250                      255  
 Gly Ile Arg Pro Ala Gly Pro Gly Arg Gly Ala Arg Arg Leu Leu Val  
                          260                      265                      270  
 Leu Glu Glu Phe Lys Thr Glu Lys Arg Leu Cys Lys Met Phe Tyr Ala  
                          275                      280                      285  
 Val Thr Leu Leu Phe Leu Leu Leu Trp Gly Pro Tyr Val Val Ala Ser  
                          290                      295                      300  
 Tyr Leu Arg Val Leu Val Arg Pro Gly Ala Val Pro Gln Ala Tyr Leu  
 305                      310                      315                      320  
 Thr Ala Ser Val Trp Leu Thr Phe Ala Gln Ala Gly Ile Asn Pro Val  
                          325                      330                      335  
 Val Cys Phe Leu Phe Asn Arg Glu Leu Arg Asp Cys Phe Arg Ala Gln  
                          340                      345                      350  
 Phe Pro Cys Cys Gln Ser Pro Arg Thr Thr Gln Ala Thr His Pro Cys  
                          355                      360                      365  
 Asp Leu Lys Gly Ile Gly Leu Ala Ser Lys Gly Glu Glu Leu Phe Thr  
                          370                      375                      380  
 Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His  
 385                      390                      395                      400  
 Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys  
                          405                      410                      415  
 Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp  
                          420                      425                      430  
 Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg  
                          435                      440                      445  
 Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro



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450                      455                      460  
 Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn  
 465                      470                      475                      480  
 Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn  
                     485                      490                      495  
 Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu  
                     500                      505                      510  
 Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met  
                     515                      520                      525  
 Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His  
                     530                      535                      540  
 Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn  
 545                      550                      555                      560  
 Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu  
                     565                      570                      575  
 Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His  
                     580                      585                      590  
 Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met  
                     595                      600                      605  
 Asp Glu Leu Tyr Asn  
                     610

&lt;210&gt; 103

&lt;211&gt; 1145

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 103

Met Asp Thr Ser Arg Leu Gly Val Leu Leu Ser Leu Pro Val Leu Leu

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	5	10	15
Gln Leu Ala Thr Gly Gly Ser Ser Pro Arg Ser Gly Val Leu Leu Arg			
20	25	30	
Gly Cys Pro Thr His Cys His Cys Glu Pro Asp Gly Arg Met Leu Leu			
35	40	45	
Arg Val Asp Cys Ser Asp Leu Gly Leu Ser Glu Leu Pro Ser Asn Leu			
50	55	60	
Ser Val Phe Thr Ser Tyr Leu Asp Leu Ser Met Asn Asn Ile Ser Gln			
65	70	75	80
Leu Leu Pro Asn Pro Leu Pro Ser Leu Arg Phe Leu Glu Glu Leu Arg			
85	90	95	
Leu Ala Gly Asn Ala Leu Thr Tyr Val Pro Lys Gly Ala Phe Thr Gly			
100	105	110	
Leu Tyr Ser Leu Lys Val Leu Met Leu Gln Asn Asn Gln Leu Arg His			
115	120	125	
Val Pro Thr Glu Ala Leu Gln Asn Leu Arg Ser Leu Gln Ser Leu Arg			
130	135	140	
Leu Asp Ala Asn His Ile Ser Tyr Val Pro Pro Ser Cys Phe Ser Gly			
145	150	155	160
Leu His Ser Leu Arg His Leu Trp Leu Asp Asp Asn Ala Leu Thr Glu			
165	170	175	
Ile Pro Val Gln Ala Phe Arg Ser Leu Ser Ala Leu Gln Ala Met Thr			
180	185	190	
Leu Ala Leu Asn Lys Ile His His Ile Pro Asp Tyr Ala Phe Gly Asn			
195	200	205	
Leu Ser Ser Leu Val Val Leu His Leu His Asn Asn Arg Ile His Ser			
210	215	220	
Leu Gly Lys Lys Cys Phe Asp Gly Leu His Ser Leu Glu Thr Leu Asp			
225	230	235	240

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Leu Asn Tyr Asn Asn Leu Asp Glu Phe Pro Thr Ala Ile Arg Thr Leu  
 245 250 255  
 Ser Asn Leu Lys Glu Leu Gly Phe His Ser Asn Asn Ile Arg Ser Ile  
 260 265 270  
 Pro Glu Lys Ala Phe Val Gly Asn Pro Ser Leu Ile Thr Ile His Phe  
 275 280 285  
 Tyr Asp Asn Pro Ile Gln Phe Val Gly Arg Ser Ala Phe Gln His Leu  
 290 295 300  
 Pro Glu Leu Arg Thr Leu Thr Leu Asn Gly Ala Ser Gln Ile Thr Glu  
 305 310 315 320  
 Phe Pro Asp Leu Thr Gly Thr Ala Asn Leu Glu Ser Leu Thr Leu Thr  
 325 330 335  
 Gly Ala Gln Ile Ser Ser Leu Pro Gln Thr Val Cys Asn Gln Leu Pro  
 340 345 350  
 Asn Leu Gln Val Leu Asp Leu Ser Tyr Asn Leu Leu Glu Asp Leu Pro  
 355 360 365  
 Ser Phe Ser Val Cys Gln Lys Leu Gln Lys Ile Asp Leu Arg His Asn  
 370 375 380  
 Glu Ile Tyr Glu Ile Lys Val Asp Thr Phe Gln Gln Leu Leu Ser Leu  
 385 390 395 400  
 Arg Ser Leu Asn Leu Ala Trp Asn Lys Ile Ala Ile Ile His Pro Asn  
 405 410 415  
 Ala Phe Ser Thr Leu Pro Ser Leu Ile Lys Leu Asp Leu Ser Ser Asn  
 420 425 430  
 Leu Leu Ser Ser Phe Pro Ile Thr Gly Leu His Gly Leu Thr His Leu  
 435 440 445  
 Lys Leu Thr Gly Asn His Ala Leu Gln Ser Leu Ile Ser Ser Glu Asn  
 450 455 460  
 Phe Pro Glu Leu Lys Val Ile Glu Met Pro Tyr Ala Tyr Gln Cys Cys

271/518

465	470	475	480
Ala Phe Gly Val Cys Glu Asn Ala Tyr Lys Ile Ser Asn Gln Trp Asn			
	485	490	495
Lys Gly Asp Asn Ser Ser Met Asp Asp Leu His Lys Lys Asp Ala Gly			
	500	505	510
Met Phe Gln Ala Gln Asp Glu Arg Asp Leu Glu Asp Phe Leu Leu Asp			
	515	520	525
Phe Glu Glu Asp Leu Lys Ala Leu His Ser Val Gln Cys Ser Pro Ser			
	530	535	540
Pro Gly Pro Phe Lys Pro Cys Glu His Leu Leu Asp Gly Trp Leu Ile			
	545	550	555
Arg Ile Gly Val Trp Thr Ile Ala Val Leu Ala Leu Thr Cys Asn Ala			
	565	570	575
Leu Val Thr Ser Thr Val Phe Arg Ser Pro Leu Tyr Ile Ser Pro Ile			
	580	585	590
Lys Leu Leu Ile Gly Val Ile Ala Ala Val Asn Met Leu Thr Gly Val			
	595	600	605
Ser Ser Ala Val Leu Ala Gly Val Asp Ala Phe Thr Phe Gly Ser Phe			
	610	615	620
Ala Arg His Gly Ala Trp Trp Glu Asn Gly Val Gly Cys His Val Ile			
	625	630	635
Gly Phe Leu Ser Ile Phe Ala Ser Glu Ser Ser Val Phe Leu Leu Thr			
	645	650	655
Leu Ala Ala Leu Glu Arg Gly Phe Ser Val Lys Tyr Ser Ala Lys Phe			
	660	665	670
Glu Thr Lys Ala Pro Phe Ser Ser Leu Lys Val Ile Ile Leu Leu Cys			
	675	680	685
Ala Leu Leu Ala Leu Thr Met Ala Ala Val Pro Leu Leu Gly Gly Ser			
	690	695	700

272/518

Lys Tyr Gly Ala Ser Pro Leu Cys Leu Pro Leu Pro Phe Gly Glu Pro  
 705                      710                      715                      720  
 Ser Thr Met Gly Tyr Met Val Ala Leu Ile Leu Leu Asn Ser Leu Cys  
                     725                      730                      735  
 Phe Leu Met Met Thr Ile Ala Tyr Thr Lys Leu Tyr Cys Asn Leu Asp  
                     740                      745                      750  
 Lys Gly Asp Leu Glu Asn Ile Trp Asp Cys Ser Met Val Lys His Ile  
                     755                      760                      765  
 Ala Leu Leu Leu Phe Thr Asn Cys Ile Leu Asn Cys Pro Val Ala Phe  
                     770                      775                      780  
 Leu Ser Phe Ser Ser Leu Ile Asn Leu Thr Phe Ile Ser Pro Glu Val  
 785                      790                      795                      800  
 Ile Lys Phe Ile Leu Leu Val Val Val Pro Leu Pro Ala Cys Leu Asn  
                     805                      810                      815  
 Pro Leu Leu Tyr Ile Leu Phe Asn Pro His Phe Lys Glu Asp Leu Val  
                     820                      825                      830  
 Ser Leu Arg Lys Gln Thr Tyr Val Trp Thr Arg Ser Lys His Pro Ser  
                     835                      840                      845  
 Leu Met Ser Ile Asn Ser Asp Asp Val Glu Lys Gln Ser Cys Asp Ser  
                     850                      855                      860  
 Thr Gln Ala Leu Val Thr Phe Thr Ser Ser Ser Ile Thr Tyr Asp Leu  
 865                      870                      875                      880  
 Pro Pro Ser Ser Val Pro Ser Pro Ala Tyr Pro Val Thr Glu Ser Cys  
                     885                      890                      895  
 His Leu Ser Ser Val Ala Phe Val Pro Cys Leu Ala Ser Lys Gly Glu  
                     900                      905                      910  
 Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp  
                     915                      920                      925  
 Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala

273/518

930	935	940	
Thr Tyr Gly Lys Leu	Thr Leu Lys Phe Ile Cys	Thr Thr Gly Lys Leu	
945	950	955	960
Pro Val Pro Trp Pro	Thr Leu Val Thr Thr Leu	Cys Tyr Gly Val Gln	
	965	970	975
Cys Phe Ser Arg Tyr	Pro Asp His Met Lys Arg	His Asp Phe Phe Lys	
	980	985	990
Ser Ala Met Pro Glu	Gly Tyr Val Gln Glu Arg	Thr Ile Phe Phe Lys	
	995	1000	1005
Asp Asp Gly Asn Tyr	Lys Thr Arg Ala Glu Val	Lys Phe Glu Gly Asp	
	1010	1015	1020
Thr Leu Val Asn Arg	Ile Glu Leu Lys Gly Ile	Asp Phe Lys Glu Asp	
	1025	1030	1035
Gly Asn Ile Leu Gly	His Lys Leu Glu Tyr Asn	Tyr Asn Ser His Asn	
	1045	1050	1055
Val Tyr Ile Met Ala	Asp Lys Gln Lys Asn Gly	Ile Lys Val Asn Phe	
	1060	1065	1070
Lys Thr Arg His Asn	Ile Glu Asp Gly Ser Val	Gln Leu Ala Asp His	
	1075	1080	1085
Tyr Gln Gln Asn Thr	Pro Ile Gly Asp Gly Pro	Val Leu Leu Pro Asp	
	1090	1095	1100
Asn His Tyr Leu Ser	Thr Gln Ser Ala Leu Ser	Lys Asp Pro Asn Glu	
	1105	1110	1115
Lys Arg Asp His Met	Val Leu Leu Glu Phe Val	Thr Ala Ala Gly Ile	
	1125	1130	1135
Thr His Gly Met Asp	Glu Leu Tyr Asn		
	1140	1145	

&lt;210&gt; 104

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&lt;211&gt; 560

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 104

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Met Asp Ser Thr Ile Pro Val Leu Gly Thr Glu Leu Thr Pro Ile Asn
      5              10              15
Gly Arg Glu Glu Thr Pro Cys Tyr Lys Gln Thr Leu Ser Phe Thr Gly
      20              25              30
Leu Thr Cys Ile Val Ser Leu Val Ala Leu Thr Gly Asn Ala Val Val
      35              40              45
Leu Trp Leu Leu Gly Cys Arg Met Arg Arg Asn Ala Val Ser Ile Tyr
      50              55              60
Ile Leu Asn Leu Val Ala Ala Asp Phe Leu Phe Leu Ser Gly His Ile
      65              70              75              80
Ile Cys Ser Pro Leu Arg Leu Ile Asn Ile Arg His Pro Ile Ser Lys
      85              90              95
Ile Leu Ser Pro Val Met Thr Phe Pro Tyr Phe Ile Gly Leu Ser Met
      100             105             110
Leu Ser Ala Ile Ser Thr Glu Arg Cys Leu Ser Ile Leu Trp Pro Ile
      115             120             125
Trp Tyr His Cys Arg Arg Pro Arg Tyr Leu Ser Ser Val Met Cys Val
      130             135             140
Leu Leu Trp Ala Leu Ser Leu Leu Arg Ser Ile Leu Glu Trp Met Phe
      145             150             155             160
Cys Asp Phe Leu Phe Ser Gly Ala Asp Ser Val Trp Cys Glu Thr Ser
      165             170             175
Asp Phe Ile Thr Ile Ala Trp Leu Val Phe Leu Cys Val Val Leu Cys
      180             185             190

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275/518

Gly Ser Ser Leu Val Leu Leu Val Arg Ile Leu Cys Gly Ser Arg Lys  
 195 200 205  
 Met Pro Leu Thr Arg Leu Tyr Val Thr Ile Leu Leu Thr Val Leu Val  
 210 215 220  
 Phe Leu Leu Cys Gly Leu Pro Phe Gly Ile Gln Trp Ala Leu Phe Ser  
 225 230 235 240  
 Arg Ile His Leu Asp Trp Lys Val Leu Phe Cys His Val His Leu Val  
 245 250 255  
 Ser Ile Phe Leu Ser Ala Leu Asn Ser Ser Ala Asn Pro Ile Ile Tyr  
 260 265 270  
 Phe Phe Val Gly Ser Phe Arg Gln Arg Gln Asn Arg Gln Asn Leu Lys  
 275 280 285  
 Leu Val Leu Gln Arg Ala Leu Gln Asp Thr Pro Glu Val Asp Glu Gly  
 290 295 300  
 Gly Gly Trp Leu Pro Gln Glu Thr Leu Glu Leu Ser Gly Ser Arg Leu  
 305 310 315 320  
 Glu Gln Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile  
 325 330 335  
 Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser  
 340 345 350  
 Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe  
 355 360 365  
 Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr  
 370 375 380  
 Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met  
 385 390 395 400  
 Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln  
 405 410 415  
 Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala



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420	425	430	
Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys			
435	440	445	
Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu			
450	455	460	
Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys			
465	470	475	480
Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly			
485	490	495	
Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp			
500	505	510	
Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala			
515	520	525	
Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu			
530	535	540	
Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn			
545	550	555	560

&lt;210&gt; 105

&lt;211&gt; 568

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 105

Met Asp Pro Thr Thr Pro Ala Trp Gly Thr Glu Ser Thr Thr Val Asn		
5	10	15
Gly Asn Asp Gln Ala Leu Leu Leu Leu Cys Gly Lys Glu Thr Leu Ile		
20	25	30
Pro Val Phe Leu Ile Leu Phe Ile Ala Leu Val Gly Leu Val Gly Asn		

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35	40	45	
Gly Phe Val Leu Trp Leu Leu Gly Phe Arg Met Arg Arg Asn Ala Phe			
50	55	60	
Ser Val Tyr Val Leu Ser Leu Ala Gly Ala Asp Phe Leu Phe Leu Cys			
65	70	75	80
Phe Gln Ile Ile Asn Cys Leu Val Tyr Leu Ser Asn Phe Phe Cys Ser			
	85	90	95
Ile Ser Ile Asn Phe Pro Ser Phe Phe Thr Thr Val Met Thr Cys Ala			
100	105	110	
Tyr Leu Ala Gly Leu Ser Met Leu Ser Thr Val Ser Thr Glu Arg Cys			
115	120	125	
Leu Ser Val Leu Trp Pro Ile Trp Tyr Arg Cys Arg Arg Pro Arg His			
130	135	140	
Leu Ser Ala Val Val Cys Val Leu Leu Trp Ala Leu Ser Leu Leu Leu			
145	150	155	160
Ser Ile Leu Glu Gly Lys Phe Cys Gly Phe Leu Phe Ser Asp Gly Asp			
	165	170	175
Ser Gly Trp Cys Gln Thr Phe Asp Phe Ile Thr Ala Ala Trp Leu Ile			
180	185	190	
Phe Leu Phe Met Val Leu Cys Gly Ser Ser Leu Ala Leu Leu Val Arg			
195	200	205	
Ile Leu Cys Gly Ser Arg Gly Leu Pro Leu Thr Arg Leu Tyr Leu Thr			
210	215	220	
Ile Leu Leu Thr Val Leu Val Phe Leu Leu Cys Gly Leu Pro Phe Gly			
225	230	235	240
Ile Gln Trp Phe Leu Ile Leu Trp Ile Trp Lys Asp Ser Asp Val Leu			
	245	250	255
Phe Cys His Ile His Pro Val Ser Val Val Leu Ser Ser Leu Asn Ser			
260	265	270	

278/518

Ser Ala Asn Pro Ile Ile Tyr Phe Phe Val Gly Ser Phe Arg Lys Gln  
 275 280 285  
 Trp Arg Leu Gln Gln Pro Ile Leu Lys Leu Ala Leu Gln Arg Ala Leu  
 290 295 300  
 Gln Asp Ile Ala Glu Val Asp His Ser Glu Gly Cys Phe Arg Gln Gly  
 305 310 315 320  
 Thr Pro Glu Met Ser Arg Ser Ser Leu Val Ala Ser Lys Gly Glu Glu  
 325 330 335  
 Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val  
 340 345 350  
 Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr  
 355 360 365  
 Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro  
 370 375 380  
 Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys  
 385 390 395 400  
 Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser  
 405 410 415  
 Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp  
 420 425 430  
 Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr  
 435 440 445  
 Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly  
 450 455 460  
 Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val  
 465 470 475 480  
 Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys  
 485 490 495  
 Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr

279/518

500	505	510
Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn		
515	520	525
His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys		
530	535	540
Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr		
545	550	555
His Gly Met Asp Glu Leu Tyr Asn		
565		

&lt;210&gt; 106

&lt;211&gt; 550

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 106

Met Met Glu Pro Arg Glu Ala Gly Gln His Val Gly Ala Ala Asn Ser		
5	10	15
Ala Gln Glu Asp Val Ala Phe Asn Leu Ile Ile Leu Ser Leu Thr Glu		
20	25	30
Gly Leu Gly Leu Gly Gly Leu Leu Gly Asn Gly Ala Val Leu Trp Leu		
35	40	45
Leu Ser Ser Asn Val Tyr Arg Asn Pro Phe Ala Ile Tyr Leu Leu Asp		
50	55	60
Val Ala Cys Ala Asp Leu Ile Phe Leu Gly Cys His Met Val Ala Ile		
65	70	75
Val Pro Asp Leu Leu Gln Gly Arg Leu Asp Phe Pro Gly Phe Val Gln		
85	90	95
Thr Ser Leu Ala Thr Leu Arg Phe Phe Cys Tyr Ile Val Gly Leu Ser		

280/518

100	105	110
Leu Leu Ala Ala Val Ser Val Glu Gln Cys Leu Ala Ala Leu Phe Pro		
115	120	125
Ala Trp Tyr Ser Cys Arg Arg Pro Arg His Leu Thr Thr Cys Val Cys		
130	135	140
Ala Leu Thr Trp Ala Leu Cys Leu Leu Leu His Leu Leu Leu Ser Ser		
145	150	155
Ala Cys Thr Gln Phe Phe Gly Glu Pro Ser Arg His Leu Cys Arg Thr		
165	170	175
Leu Trp Leu Val Ala Ala Val Leu Leu Ala Leu Leu Cys Cys Thr Met		
180	185	190
Cys Gly Ala Ser Leu Met Leu Leu Leu Arg Val Glu Arg Gly Pro Gln		
195	200	205
Arg Pro Pro Pro Arg Gly Phe Pro Gly Leu Ile Leu Leu Thr Val Leu		
210	215	220
Leu Phe Leu Phe Cys Gly Leu Pro Phe Gly Ile Tyr Trp Leu Ser Arg		
225	230	235
Asn Leu Leu Trp Tyr Ile Pro His Tyr Phe Tyr His Phe Ser Phe Leu		
245	250	255
Met Ala Ala Val His Cys Ala Ala Lys Pro Val Val Tyr Phe Cys Leu		
260	265	270
Gly Ser Ala Gln Gly Arg Arg Leu Pro Leu Arg Leu Val Leu Gln Arg		
275	280	285
Ala Leu Gly Asp Glu Ala Glu Leu Gly Ala Val Arg Glu Thr Ser Arg		
290	295	300
Arg Gly Leu Val Asp Ile Ala Ala Ala Ser Lys Gly Glu Glu Leu Phe		
305	310	315
Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly		
325	330	335

281/518

His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly  
                   340                  345                  350  
 Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro  
                   355                  360                  365  
 Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser  
                   370                  375                  380  
 Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met  
 385                  390                  395                  400  
 Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly  
                   405                  410                  415  
 Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val  
                   420                  425                  430  
 Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile  
                   435                  440                  445  
 Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile  
                   450                  455                  460  
 Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg  
 465                  470                  475                  480  
 His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln  
                   485                  490                  495  
 Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr  
                   500                  505                  510  
 Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp  
                   515                  520                  525  
 His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly  
                   530                  535                  540  
 Met Asp Glu Leu Tyr Asn  
 545                  550

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&lt;210&gt; 107

&lt;211&gt; 561

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 107

Met Pro Leu Pro Val Pro Pro Ala Gly Ala Gln Lys Thr Pro Glu Asp  
                           5                          10                          15  
 His Val Cys Leu His Leu Ala Gly Pro Ser Pro Ala Pro Ser Glu Pro  
                           20                          25                          30  
 Ala Arg Met Phe Gly Leu Phe Gly Leu Trp Arg Thr Phe Asp Ser Val  
                           35                          40                          45  
 Val Phe Tyr Leu Thr Leu Ile Val Gly Leu Gly Gly Pro Val Gly Asn  
                           50                          55                          60  
 Gly Leu Val Leu Trp Asn Leu Gly Phe Arg Ile Lys Lys Gly Pro Phe  
                           65                          70                          75                          80  
 Ser Ile Tyr Leu Leu His Leu Ala Ala Ala Asp Phe Leu Phe Leu Ser  
                           85                          90                          95  
 Cys Arg Val Gly Phe Ser Val Ala Gln Ala Ala Leu Gly Ala Gln Asp  
                           100                          105                          110  
 Thr Leu Tyr Phe Val Leu Thr Phe Leu Trp Phe Ala Val Gly Leu Trp  
                           115                          120                          125  
 Leu Leu Ala Ala Phe Ser Val Glu Arg Cys Leu Ser Asp Leu Phe Pro  
                           130                          135                          140  
 Ala Cys Tyr Gln Gly Cys Arg Pro Arg His Ala Ser Ala Val Leu Cys  
                           145                          150                          155                          160  
 Ala Leu Val Trp Thr Pro Thr Leu Pro Ala Val Pro Leu Pro Ala Asn  
                           165                          170                          175  
 Ala Cys Gly Leu Leu Arg Asn Ser Ala Cys Pro Leu Val Cys Pro Arg

283/518

180	185	190
Tyr His Val Ala Ser Val Thr Trp Phe Leu Val Leu Ala Arg Val Ala		
195	200	205
Trp Thr Ala Gly Val Val Leu Phe Val Trp Val Thr Cys Cys Ser Thr		
210	215	220
Arg Pro Arg Pro Arg Leu Tyr Gly Ile Val Leu Gly Ala Leu Leu Leu		
225	230	235
Leu Phe Phe Cys Gly Leu Pro Ser Val Phe Tyr Trp Ser Leu Gln Pro		
245	250	255
Leu Leu Asn Phe Leu Leu Pro Val Phe Ser Pro Leu Ala Thr Leu Leu		
260	265	270
Ala Cys Val Asn Ser Ser Ser Lys Pro Leu Ile Tyr Ser Gly Leu Gly		
275	280	285
Arg Gln Pro Gly Lys Arg Glu Pro Leu Arg Ser Val Leu Arg Arg Ala		
290	295	300
Leu Gly Glu Gly Ala Glu Leu Gly Ala Arg Gly Gln Ser Leu Pro Met		
305	310	315
Gly Leu Leu Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro		
325	330	335
Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val		
340	345	350
Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys		
355	360	365
Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val		
370	375	380
Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His		
385	390	395
Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val		
405	410	415



284/518

Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg  
 420 425 430  
 Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu  
 435 440 445  
 Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu  
 450 455 460  
 Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln  
 465 470 475 480  
 Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp  
 485 490 495  
 Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly  
 500 505 510  
 Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser  
 515 520 525  
 Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu  
 530 535 540  
 Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr  
 545 550 555 560  
 Asn

&lt;210&gt; 108

&lt;211&gt; 591

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 108

Met Glu His Thr His Ala His Leu Ala Ala Asn Ser Ser Leu Ser Trp  
 5 10 15  
 Trp Ser Pro Gly Ser Ala Cys Gly Leu Gly Phe Val Pro Val Val Tyr

285/518

20	25	30
Tyr Ser. Leu Leu Leu Cys Leu Gly Leu Pro Ala Asn Ile Leu Thr Val		
35	40	45
Ile Ile Leu Ser Gln Leu Val Ala Arg Arg Gln Lys Ser Ser Tyr Asn		
50	55	60
Tyr Leu Leu Ala Leu Ala Ala Ala Asp Ile Leu Val Leu Phe Phe Ile		
65	70	75
Val Phe Val Asp Phe Leu Leu Glu Asp Phe Ile Leu Asn Met Gln Met		
85	90	95
Pro Gln Val Pro Asp Lys Ile Ile Glu Val Leu Glu Phe Ser Ser Ile		
100	105	110
His Thr Ser Ile Trp Ile Thr Val Pro Leu Thr Ile Asp Arg Tyr Ile		
115	120	125
Ala Val Cys His Pro Leu Lys Tyr His Thr Val Ser Tyr Pro Ala Arg		
130	135	140
Thr Arg Lys Val Ile Val Ser Val Tyr Ile Thr Cys Phe Leu Thr Ser		
145	150	155
Ile Pro Tyr Tyr Trp Trp Pro Asn Ile Trp Thr Glu Asp Tyr Ile Ser		
165	170	175
Thr Ser Val His His Val Leu Ile Trp Ile His Cys Phe Thr Val Tyr		
180	185	190
Leu Val Pro Cys Ser Ile Phe Phe Ile Leu Asn Ser Ile Ile Val Tyr		
195	200	205
Lys Leu Arg Arg Lys Ser Asn Phe Arg Leu Arg Gly Tyr Ser Thr Gly		
210	215	220
Lys Thr Thr Ala Ile Leu Phe Thr Ile Thr Ser Ile Phe Ala Thr Leu		
225	230	235
Trp Ala Pro Arg Ile Ile Met Ile Leu Tyr His Leu Tyr Gly Ala Pro		
245	250	255

286/518

Ile Gln Asn Arg Trp Leu Val His Ile Met Ser Asp Ile Ala Asn Met  
 260 265 270  
 Leu Ala Leu Leu Asn Thr Ala Ile Asn Phe Phe Leu Tyr Cys Phe Ile  
 275 280 285  
 Ser Lys Arg Phe Arg Thr Met Ala Ala Ala Thr Leu Lys Ala Phe Phe  
 290 295 300  
 Lys Cys Gln Lys Gln Pro Val Gln Phe Tyr Thr Asn His Asn Phe Ser  
 305 310 315 320  
 Ile Thr Ser Ser Pro Trp Ile Ser Pro Ala Asn Ser His Cys Ile Lys  
 325 330 335  
 Met Leu Val Tyr Gln Tyr Asp Lys Asn Gly Lys Pro Ile Lys Val Ser  
 340 345 350  
 Pro Ser Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu  
 355 360 365  
 Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly  
 370 375 380  
 Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile  
 385 390 395 400  
 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr  
 405 410 415  
 Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys  
 420 425 430  
 Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu  
 435 440 445  
 Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu  
 450 455 460  
 Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly  
 465 470 475 480  
 Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr

287/518

	485		490		495
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn					
	500		505		510
Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser					
	515		520		525
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly					
	530		535		540
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu					
	545		550		555
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe					
	565		570		575
Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn					
	580		585		590

&lt;210&gt; 109

&lt;211&gt; 596

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 109

Met Pro Ser Val Ser Pro Ala Gly Pro Ser Ala Gly Ala Val Pro Asn			
	5	10	15
Ala Thr Ala Val Thr Thr Val Arg Thr Asn Ala Ser Gly Leu Glu Val			
	20	25	30
Pro Leu Phe His Leu Phe Ala Arg Leu Asp Glu Glu Leu His Gly Thr			
	35	40	45
Phe Pro Gly Leu Trp Leu Ala Leu Met Ala Val His Gly Ala Ile Phe			
	50	55	60
Leu Ala Gly Leu Val Leu Asn Gly Leu Ala Leu Tyr Val Phe Cys Cys			

288/518

65	70	75	80
Arg Thr Arg Ala Lys Thr Pro Ser Val Ile Tyr Thr Ile Asn Leu Val			
85	90	95	
Val Thr Asp Leu Leu Val Gly Leu Ser Leu Pro Thr Arg Phe Ala Val			
100	105	110	
Tyr Tyr Gly Ala Arg Gly Cys Leu Arg Cys Ala Phe Pro His Val Leu			
115	120	125	
Gly Tyr Phe Leu Asn Met His Cys Ser Ile Leu Phe Leu Thr Cys Ile			
130	135	140	
Cys Val Asp Arg Tyr Leu Ala Ile Val Arg Pro Glu Gly Ser Arg Arg			
145	150	155	160
Cys Arg Gln Pro Ala Cys Ala Arg Ala Val Cys Ala Phe Val Trp Leu			
165	170	175	
Ala Ala Gly Ala Val Thr Leu Ser Val Leu Gly Val Thr Gly Ser Arg			
180	185	190	
Pro Cys Cys Arg Val Phe Ala Leu Thr Val Leu Glu Phe Leu Leu Pro			
195	200	205	
Leu Leu Val Ile Ser Val Phe Thr Gly Arg Ile Met Cys Ala Leu Ser			
210	215	220	
Arg Pro Gly Leu Leu Arg Gln Gly Arg Gln Arg Arg Val Arg Ala Met			
225	230	235	240
Gln Leu Leu Leu Thr Val Leu Ile Ile Phe Leu Val Cys Phe Thr Pro			
245	250	255	
Phe His Ala Arg Gln Val Ala Val Ala Leu Trp Pro Asp Met Pro His			
260	265	270	
His Thr Ser Leu Val Val Tyr His Val Ala Val Thr Leu Ser Ser Leu			
275	280	285	
Asn Ser Cys Met Asp Pro Ile Val Tyr Cys Phe Val Thr Ser Gly Phe			
290	295	300	

289/518

Gln Ala Thr Val Arg Gly Leu Phe Gly Gln His Gly Glu Arg Glu Pro  
 305                      310                      315                      320  
 Ser Ser Gly Asp Val Val Ser Met His Arg Ser Ser Lys Gly Ser Gly  
                          325                      330                      335  
 Arg His His Ile Leu Ser Ala Gly Pro His Ala Leu Thr Gln Ala Leu  
                          340                      345                      350  
 Ala Asn Gly Pro Glu Ala Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly  
                          355                      360                      365  
 Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys  
                          370                      375                      380  
 Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu  
 385                      390                      395                      400  
 Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro  
                          405                      410                      415  
 Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr  
                          420                      425                      430  
 Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu  
                          435                      440                      445  
 Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr  
                          450                      455                      460  
 Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg  
 465                      470                      475                      480  
 Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly  
                          485                      490                      495  
 His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala  
                          500                      505                      510  
 Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn  
                          515                      520                      525  
 Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr

290/518

530                      535                      540  
 Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser  
 545                      550                      555                      560  
 Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met  
                     565                      570                      575  
 Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp  
                     580                      585                      590  
 Glu Leu Tyr Asn  
                     595

<210> 110  
 <211> 543  
 <212> PRT  
 <213> Human

<400> 110  
 Met Pro Gly His Asn Thr Ser Arg Asn Ser Ser Cys Asp Pro Ile Val  
                     5                      10                      15  
 Thr Pro His Leu Ile Ser Leu Tyr Phe Ile Val Leu Ile Gly Gly Leu  
                     20                      25                      30  
 Val Gly Val Ile Ser Ile Leu Phe Leu Leu Val Lys Met Asn Thr Arg  
                     35                      40                      45  
 Ser Val Thr Thr Met Ala Val Ile Asn Leu Val Val Val His Ser Val  
                     50                      55                      60  
 Phe Leu Leu Thr Val Pro Phe Arg Leu Thr Tyr Leu Ile Lys Lys Thr  
                     65                      70                      75                      80  
 Trp Met Phe Gly Leu Pro Phe Cys Lys Phe Val Ser Ala Met Leu His  
                     85                      90                      95  
 Ile His Met Tyr Leu Thr Phe Leu Phe Tyr Val Val Ile Leu Val Thr

291/518

100	105	110	
Arg Tyr Leu Ile Phe Phe Lys Cys Lys Asp Lys Val Glu Phe Tyr Arg			
115	120	125	
Lys Leu His Ala Val Ala Ala Ser Ala Gly Met Trp Thr Leu Val Ile			
130	135	140	
Val Ile Val Val Pro Leu Val Val Ser Arg Tyr Gly Ile His Glu Glu			
145	150	155	160
Tyr Asn Glu Glu His Cys Phe Lys Phe His Lys Glu Leu Ala Tyr Thr			
165	170	175	
Tyr Val Lys Ile Ile Asn Tyr Met Ile Val Ile Phe Val Ile Ala Val			
180	185	190	
Ala Val Ile Leu Leu Val Phe Gln Val Phe Ile Ile Met Leu Met Val			
195	200	205	
Gln Lys Leu Arg His Ser Leu Leu Ser His Gln Glu Phe Trp Ala Gln			
210	215	220	
Leu Lys Asn Leu Phe Phe Ile Gly Val Ile Leu Val Cys Phe Leu Pro			
225	230	235	240
Tyr Gln Phe Phe Arg Ile Tyr Tyr Leu Asn Val Val Thr His Ser Asn			
245	250	255	
Ala Cys Asn Ser Lys Val Ala Phe Tyr Asn Glu Ile Phe Leu Ser Val			
260	265	270	
Thr Ala Ile Ser Cys Tyr Asp Leu Leu Leu Phe Val Phe Gly Gly Ser			
275	280	285	
His Trp Phe Lys Gln Lys Ile Ile Gly Leu Trp Asn Cys Val Leu Cys			
290	295	300	
Arg Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu			
305	310	315	320
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly			
325	330	335	



292/518

Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile  
 340 345 350  
 Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr  
 355 360 365  
 Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys  
 370 375 380  
 Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu  
 385 390 395 400  
 Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu  
 405 410 415  
 Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly  
 420 425 430  
 Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr  
 435 440 445  
 Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn  
 450 455 460  
 Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser  
 465 470 475 480  
 Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly  
 485 490 495  
 Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu  
 500 505 510  
 Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe  
 515 520 525  
 Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
 530 535 540

&lt;210&gt; 111

&lt;211&gt; 577

293/518

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 111

Met	Asn	Glu	Pro	Leu	Asp	Tyr	Leu	Ala	Asn	Ala	Ser	Asp	Phe	Pro	Asp
			5						10					15	
Tyr	Ala	Ala	Ala	Phe	Gly	Asn	Cys	Thr	Asp	Glu	Asn	Ile	Pro	Leu	Lys
			20					25					30		
Met	His	Tyr	Leu	Pro	Val	Ile	Tyr	Gly	Ile	Ile	Phe	Leu	Val	Gly	Phe
			35					40				45			
Pro	Gly	Asn	Ala	Val	Val	Ile	Ser	Thr	Tyr	Ile	Phe	Lys	Met	Arg	Pro
			50				55					60			
Trp	Lys	Ser	Ser	Thr	Ile	Ile	Met	Leu	Asn	Leu	Ala	Cys	Thr	Asp	Leu
			65			70				75				80	
Leu	Tyr	Leu	Thr	Ser	Leu	Pro	Phe	Leu	Ile	His	Tyr	Tyr	Ala	Ser	Gly
				85					90					95	
Glu	Asn	Trp	Ile	Phe	Gly	Asp	Phe	Met	Cys	Lys	Phe	Ile	Arg	Phe	Ser
			100					105					110		
Phe	His	Phe	Asn	Leu	Tyr	Ser	Ser	Ile	Leu	Phe	Leu	Thr	Cys	Phe	Ser
			115					120					125		
Ile	Phe	Arg	Tyr	Cys	Val	Ile	Ile	His	Pro	Met	Ser	Cys	Phe	Ser	Ile
			130				135					140			
His	Lys	Thr	Arg	Cys	Ala	Val	Val	Ala	Cys	Ala	Val	Val	Trp	Ile	Ile
			145			150				155				160	
Ser	Leu	Val	Ala	Val	Ile	Pro	Met	Thr	Phe	Leu	Ile	Thr	Ser	Thr	Asn
				165					170					175	
Arg	Thr	Asn	Arg	Ser	Ala	Cys	Leu	Asp	Leu	Thr	Ser	Ser	Asp	Glu	Leu
			180						185					190	
Asn	Thr	Ile	Lys	Trp	Tyr	Asn	Leu	Ile	Leu	Thr	Ala	Thr	Thr	Phe	Cys

294/518

195	200	205
Leu Pro Leu Val Ile Val Thr Leu Cys Tyr Thr Thr Ile Ile His Thr		
210	215	220
Leu Thr His Gly Leu Gln Thr Asp Ser Cys Leu Lys Gln Lys Ala Arg		
225	230	235
Arg Leu Thr Ile Leu Leu Leu Leu Ala Phe Tyr Val Cys Phe Leu Pro		
245	250	255
Phe His Ile Leu Arg Val Ile Arg Ile Glu Ser Arg Leu Leu Ser Ile		
260	265	270
Ser Cys Ser Ile Glu Asn Gln Ile His Glu Ala Tyr Ile Val Ser Arg		
275	280	285
Pro Leu Ala Ala Leu Asn Thr Phe Gly Asn Leu Leu Leu Tyr Val Val		
290	295	300
Val Ser Asp Asn Phe Gln Gln Ala Val Cys Ser Thr Val Arg Cys Lys		
305	310	315
Val Ser Gly Asn Leu Glu Gln Ala Lys Lys Ile Ser Tyr Ser Asn Asn		
325	330	335
Pro Ala Ser Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro		
340	345	350
Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val		
355	360	365
Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys		
370	375	380
Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val		
385	390	395
Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe*Ser Arg Tyr Pro Asp His		
405	410	415
Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val		
420	425	430

295/518

Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg  
           435                    440                    445  
 Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu  
           450                    455                    460  
 Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu  
 465                    470                    475                    480  
 Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln  
                     485                    490                    495  
 Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp  
                     500                    505                    510  
 Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly  
           515                    520                    525  
 Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser  
           530                    535                    540  
 Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu  
 545                    550                    555                    560  
 Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr  
                     565                    570                    575

Asn

&lt;210&gt; 112

&lt;211&gt; 569

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 112

Met Ile Thr Leu Asn Asn Gln Asp Gln Pro Val Pro Phe Asn Ser Ser  
                     5                    10                    15  
 His Pro Asp Glu Tyr Lys Ile Ala Ala Leu Val Phe Tyr Ser Cys Ile

296/518

	20		25		30
Phe	Ile	Ile	Gly	Leu	Phe
	35		40		45
Cys	Thr	Thr	Lys	Lys	Arg
	50		55		60
Ala	Leu	Val	Asp	Leu	Ile
	65		70		75
Tyr	Tyr	Ala	Lys	Asp	Glu
			85		90
Leu	Gly	Ala	Leu	Thr	Val
			100		105
Ala	Phe	Ile	Ser	Ala	Asp
	115		120		125
Ala	Lys	Glu	Leu	Lys	Asn
	130		135		140
Val	Trp	Ile	Met	Thr	Leu
	145		150		155
Lys	Asp	Pro	Asp	Lys	Asp
			165		170
Asp	Ile	Ile	Tyr	Leu	Lys
			180		185
Thr	Phe	Phe	Phe	Leu	Ile
	195		200		205
Val	Ile	Ile	His	Asn	Leu
	210		215		220
Lys	Val	Lys	Glu	Lys	Ser
	225		230		235
Val	Leu	Val	Cys	Phe	Met
			245		250
					255

297/518

Leu Gly Thr Gly Glu Asn Ser Tyr Asn Pro Trp Gly Ala Phe Thr Thr  
                   260                                  265                                  270  
 Phe Leu Met Asn Leu Ser Thr Cys Leu Asp Val Ile Leu Tyr Tyr Ile  
                   275                                  280                                  285  
 Val Ser Lys Gln Phe Gln Ala Arg Val Ile Ser Val Met Leu Tyr Arg  
                   290                                  295                                  300  
 Asn Tyr Leu Arg Ser Met Arg Arg Lys Ser Phe Arg Ser Gly Ser Leu  
 305                                  310                                  315                                  320  
 Arg Ser Leu Ser Asn Ile Asn Ser Glu Met Leu Ala Ser Lys Gly Glu  
                                   325                                  330                                  335  
 Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp  
                   340                                  345                                  350  
 Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala  
                   355                                  360                                  365  
 Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu  
                   370                                  375                                  380  
 Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln  
 385                                  390                                  395                                  400  
 Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys  
                                   405                                  410                                  415  
 Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys  
                   420                                  425                                  430  
 Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp  
                   435                                  440                                  445  
 Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp  
                   450                                  455                                  460  
 Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn  
 465                                  470                                  475                                  480  
 Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe

298/518

	485		490		495
Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His					
	500		505		510
Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp					
	515		520		525
Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu					
	530		535		540
Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile					
	545		550		555
Thr His Gly Met Asp Glu Leu Tyr Asn					560
	565				

&lt;210&gt; 113

&lt;211&gt; 787

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 113

Met Ala Thr Pro Arg Gly Leu Gly Ala Leu Leu Leu Leu Leu Leu			
	5	10	15
Pro Thr Ser Gly Gln Glu Lys Pro Thr Glu Gly Pro Arg Asn Thr Cys			
	20	25	30
Leu Gly Ser Asn Asn Met Tyr Asp Ile Phe Asn Leu Asn Asp Lys Ala			
	35	40	45
Leu Cys Phe Thr Lys Cys Arg Gln Ser Gly Ser Asp Ser Cys Asn Val			
	50	55	60
Glu Asn Leu Gln Arg Tyr Trp Leu Asn Tyr Glu Ala His Leu Met Lys			
	65	70	75
Glu Gly Leu Thr Gln Lys Val Asn Thr Pro Phe Leu Lys Ala Leu Val			80

299/518

	85	90	95
Gln Asn Leu Ser Thr Asn Thr Ala Glu Asp Phe Tyr Phe Ser Leu Glu			
100	105	110	
Pro Ser Gln Val Pro Arg Gln Val Met Lys Asp Glu Asp Lys Pro Pro			
115	120	125	
Asp Arg Val Arg Leu Pro Lys Ser Leu Phe Arg Ser Leu Pro Gly Asn			
130	135	140	
Arg Ser Val Val Arg Leu Ala Val Thr Ile Leu Asp Ile Gly Pro Gly			
145	150	155	160
Thr Leu Phe Lys Gly Pro Arg Leu Gly Leu Gly Asp Gly Ser Gly Val			
165	170	175	
Leu Asn Asn Arg Leu Val Gly Leu Ser Val Gly Gln Met His Val Thr			
180	185	190	
Lys Leu Ala Glu Pro Leu Glu Ile Val Phe Ser His Gln Arg Pro Pro			
195	200	205	
Pro Asn Met Thr Leu Thr Cys Val Phe Trp Asp Val Thr Lys Gly Thr			
210	215	220	
Thr Gly Asp Trp Ser Ser Glu Gly Cys Ser Thr Glu Val Arg Pro Glu			
225	230	235	240
Gly Thr Val Cys Cys Cys Asp His Leu Thr Phe Phe Ala Leu Leu Leu			
245	250	255	
Arg Pro Thr Leu Asp Gln Ser Thr Val His Ile Leu Thr Arg Ile Ser			
260	265	270	
Gln Ala Gly Cys Gly Val Ser Met Ile Phe Leu Ala Phe Thr Ile Ile			
275	280	285	
Leu Tyr Ala Phe Leu Arg Leu Ser Arg Glu Arg Phe Lys Ser Glu Asp			
290	295	300	
Ala Pro Lys Ile His Val Ala Leu Gly Gly Ser Leu Phe Leu Leu Asn			
305	310	315	320



300/518

Leu Ala Phe Leu Val Asn Val Gly Ser Gly Ser Lys Gly Ser Asp Ala  
 325 330 335  
 Ala Cys Trp Ala Arg Gly Ala Val Phe His Tyr Phe Leu Leu Cys Ala  
 340 345 350  
 Phe Thr Trp Met Gly Leu Glu Ala Phe His Leu Tyr Leu Leu Ala Val  
 355 360 365  
 Arg Val Phe Asn Thr Tyr Phe Gly His Tyr Phe Leu Lys Leu Ser Leu  
 370 375 380  
 Val Gly Trp Gly Leu Pro Ala Leu Met Val Ile Gly Thr Gly Ser Ala  
 385 390 395 400  
 Asn Ser Tyr Gly Leu Tyr Thr Ile Arg Asp Arg Glu Asn Arg Thr Ser  
 405 410 415  
 Leu Glu Leu Cys Trp Phe Arg Glu Gly Thr Thr Met Tyr Ala Leu Tyr  
 420 425 430  
 Ile Thr Val His Gly Tyr Phe Leu Ile Thr Phe Leu Phe Gly Met Val  
 435 440 445  
 Val Leu Ala Leu Val Val Trp Lys Ile Phe Thr Leu Ser Arg Ala Thr  
 450 455 460  
 Ala Val Lys Glu Arg Gly Lys Asn Arg Lys Lys Val Leu Thr Leu Leu  
 465 470 475 480  
 Gly Leu Ser Ser Leu Val Gly Val Thr Trp Gly Leu Ala Ile Phe Thr  
 485 490 495  
 Pro Leu Gly Leu Ser Thr Val Tyr Ile Phe Ala Leu Phe Asn Ser Leu  
 500 505 510  
 Gln Gly Val Phe Ile Cys Cys Trp Phe Thr Ile Leu Tyr Leu Pro Ser  
 515 520 525  
 Gln Ser Thr Thr Val Ser Ser Ser Thr Ala Arg Leu Asp Gln Ala His  
 530 535 540  
 Ser Ala Ser Gln Glu Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val

301/518

545	550	555	560
Val Pro Ile Leu Val	Glu Leu Asp Gly Asp	Val Asn Gly His Lys Phe	
	565	570	575
Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr			
	580	585	590
Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr			
	595	600	605
Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro			
	610	615	620
Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly			
625	630	635	640
Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys			
	645	650	655
Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile			
	660	665	670
Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His			
	675	680	685
Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp			
	690	695	700
Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile			
705	710	715	720
Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro			
	725	730	735
Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr			
	740	745	750
Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val			
	755	760	765
Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu			
	770	775	780

302/518

Leu Tyr Asn

785

&lt;210&gt; 114

&lt;211&gt; 608

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 114

Met Gly Asp Arg Arg Phe Ile Asp Phe Gln Phe Gln Asp Ser Asn Ser

5

10

15

Ser Leu Arg Pro Arg Leu Gly Asn Ala Thr Ala Asn Asn Thr Cys Ile

20

25

30

Val Asp Asp Ser Phe Lys Tyr Asn Leu Asn Gly Ala Val Tyr Ser Val

35

40

45

Val Phe Ile Leu Gly Leu Ile Thr Asn Ser Val Ser Leu Phe Val Phe

50

55

60

Cys Phe Arg Met Lys Met Arg Ser Glu Thr Ala Ile Phe Ile Thr Asn

65

70

75

80

Leu Ala Val Ser Asp Leu Leu Phe Val Cys Thr Leu Pro Phe Lys Ile

85

90

95

Phe Tyr Asn Phe Asn Arg His Trp Pro Phe Gly Asp Thr Leu Cys Lys

100

105

110

Ile Ser Gly Thr Ala Phe Leu Thr Asn Ile Tyr Gly Ser Met Leu Phe

115

120

125

Leu Thr Cys Ile Ser Val Asp Arg Phe Leu Ala Ile Val Tyr Pro Phe

130

135

140

Arg Ser Arg Thr Ile Arg Thr Arg Arg Asn Ser Ala Ile Val Cys Ala

145

150

155

160

303/518

Gly Val Trp Ile Leu Val Leu Ser Gly Gly Ile Ser Ala Ser Leu Phe  
 165 170 175  
 Ser Thr Thr Asn Val Asn Asn Ala Thr Thr Thr Cys Phe Glu Gly Phe  
 180 185 190  
 Ser Lys Arg Val Trp Lys Thr Tyr Leu Ser Lys Ile Thr Ile Phe Ile  
 195 200 205  
 Glu Val Val Gly Phe Ile Ile Pro Leu Ile Leu Asn Val Ser Cys Ser  
 210 215 220  
 Ser Val Val Leu Arg Thr Leu Arg Lys Pro Ala Thr Leu Ser Gln Ile  
 225 230 235 240  
 Gly Thr Asn Lys Lys Lys Val Leu Lys Met Ile Thr Val His Met Ala  
 245 250 255  
 Val Phe Val Val Cys Phe Val Pro Tyr Asn Ser Val Leu Phe Leu Tyr  
 260 265 270  
 Ala Leu Val Arg Ser Gln Ala Ile Thr Asn Cys Phe Leu Glu Arg Phe  
 275 280 285  
 Ala Lys Ile Met Tyr Pro Ile Thr Leu Cys Leu Ala Thr Leu Asn Cys  
 290 295 300  
 Cys Phe Asp Pro Phe Ile Tyr Tyr Phe Thr Leu Glu Ser Phe Gln Lys  
 305 310 315 320  
 Ser Phe Tyr Ile Asn Ala His Ile Arg Met Glu Ser Leu Phe Lys Thr  
 325 330 335  
 Glu Thr Pro Leu Thr Thr Lys Pro Ser Leu Pro Ala Ile Gln Glu Glu  
 340 345 350  
 Val Ser Asp Gln Thr Thr Asn Asn Gly Gly Glu Leu Met Leu Glu Ser  
 355 360 365  
 Thr Phe Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile  
 370 375 380  
 Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser

304/518

385	390	395	400
Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe			
405	410	415	
Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr			
420	425	430	
Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met			
435	440	445	
Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln			
450	455	460	
Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala			
465	470	475	480
Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys			
485	490	495	
Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu			
500	505	510	
Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys			
515	520	525	
Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly			
530	535	540	
Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp			
545	550	555	560
Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala			
565	570	575	
Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu			
580	585	590	
Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn			
595	600	605	

&lt;210&gt; 115

305/518

&lt;211&gt; 577

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 115

Met	Ala	Asn	Leu	Asp	Lys	Tyr	Thr	Glu	Thr	Phe	Lys	Met	Gly	Ser	Asn
			5						10					15	
Ser	Thr	Ser	Thr	Ala	Glu	Ile	Tyr	Cys	Asn	Val	Thr	Asn	Val	Lys	Phe
			20					25					30		
Gln	Tyr	Ser	Leu	Tyr	Ala	Thr	Thr	Tyr	Ile	Leu	Ile	Phe	Ile	Pro	Gly
			35					40					45		
Leu	Leu	Ala	Asn	Ser	Ala	Ala	Leu	Trp	Val	Leu	Cys	Arg	Phe	Ile	Ser
			50				55					60			
Lys	Lys	Asn	Lys	Ala	Ile	Ile	Phe	Met	Ile	Asn	Leu	Ser	Val	Ala	Asp
			65			70				75				80	
Leu	Ala	His	Val	Leu	Ser	Leu	Pro	Leu	Arg	Ile	Tyr	Tyr	Tyr	Ile	Ser
				85					90					95	
His	His	Trp	Pro	Phe	Gln	Arg	Ala	Leu	Cys	Leu	Leu	Cys	Phe	Tyr	Leu
			100					105					110		
Lys	Tyr	Leu	Asn	Met	Tyr	Ala	Ser	Ile	Cys	Phe	Leu	Thr	Cys	Ile	Ser
			115					120					125		
Leu	Gln	Arg	Cys	Phe	Phe	Leu	Leu	Lys	Pro	Phe	Arg	Ala	Arg	Asp	Trp
			130				135					140			
Lys	Arg	Arg	Tyr	Asp	Val	Gly	Ile	Ser	Ala	Ala	Ile	Trp	Ile	Val	Val
			145			150				155				160	
Gly	Thr	Ala	Cys	Leu	Pro	Phe	Pro	Ile	Leu	Arg	Ser	Thr	Asp	Leu	Asn
				165					170					175	
Asn	Asn	Lys	Ser	Cys	Phe	Ala	Asp	Leu	Gly	Tyr	Lys	Gln	Met	Asn	Ala
			180					185					190		

306/518

Val Ala Leu Val Gly Met Ile Thr Val Ala Glu Leu Ala Gly Phe Val  
 195 200 205  
 Ile Pro Val Ile Ile Ile Ala Trp Cys Thr Trp Lys Thr Thr Ile Ser  
 210 215 220  
 Leu Arg Gln Pro Pro Met Ala Phe Gln Gly Ile Ser Glu Arg Gln Lys  
 225 230 235 240  
 Ala Leu Arg Met Val Phe Met Cys Ala Ala Val Phe Phe Ile Cys Phe  
 245 250 255  
 Thr Pro Tyr His Ile Asn Phe Ile Phe Tyr Thr Met Val Lys Glu Thr  
 260 265 270  
 Ile Ile Ser Ser Cys Pro Val Val Arg Ile Ala Leu Tyr Phe His Pro  
 275 280 285  
 Phe Cys Leu Cys Leu Ala Ser Leu Cys Cys Leu Leu Asp Pro Ile Leu  
 290 295 300  
 Tyr Tyr Phe Met Ala Ser Glu Phe Arg Asp Gln Leu Ser Arg His Gly  
 305 310 315 320  
 Ser Ser Val Thr Arg Ser Arg Leu Met Ser Lys Glu Ser Gly Ser Ser  
 325 330 335  
 Met Ile Gly Ser Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro  
 340 345 350  
 Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val  
 355 360 365  
 Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys  
 370 375 380  
 Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val  
 385 390 395 400  
 Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His  
 405 410 415  
 Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val

307/518

420	425	430	
Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg			
435	440	445	
Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu			
450	455	460	
Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu			
465	470	475	480
Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln			
485	490	495	
Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp			
500	505	510	
Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly			
515	520	525	
Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser			
530	535	540	
Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu			
545	550	555	560
Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr			
565	570	575	
Asn			

&lt;210&gt; 116

&lt;211&gt; 851

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 116

Met Arg Ala Pro Gly Ala Leu Leu Ala Arg Met Ser Arg Leu Leu Leu

5

10

15



308/518

Leu Leu Leu Leu Lys Val Ser Ala Ser Ser Ala Leu Gly Val Ala Pro  
                   20                                  25                                  30  
 Ala Ser Arg Asn Glu Thr Cys Leu Gly Glu Ser Cys Ala Pro Thr Val  
                   35                                  40                                  45  
 Ile Gln Arg Arg Gly Arg Asp Ala Trp Gly Pro Gly Asn Ser Ala Arg  
                   50                                  55                                  60  
 Asp Val Leu Arg Ala Arg Ala Pro Arg Glu Glu Gln Gly Ala Ala Phe  
                   65                                  70                                  75                                  80  
 Leu Ala Gly Pro Ser Trp Asp Leu Pro Ala Ala Pro Gly Arg Asp Pro  
                                   85                                  90                                  95  
 Ala Ala Gly Arg Gly Ala Glu Ala Ser Ala Ala Gly Pro Pro Gly Pro  
                   100                                  105                                  110  
 Pro Thr Arg Pro Pro Gly Pro Trp Arg Trp Lys Gly Ala Arg Gly Gln  
                   115                                  120                                  125  
 Glu Pro Ser Glu Thr Leu Gly Arg Gly Asn Pro Thr Ala Leu Gln Leu  
                   130                                  135                                  140  
 Phe Leu Gln Ile Ser Glu Glu Glu Glu Lys Gly Pro Arg Gly Ala Gly  
                   145                                  150                                  155                                  160  
 Ile Ser Gly Arg Ser Gln Glu Gln Ser Val Lys Thr Val Pro Gly Ala  
                                   165                                  170                                  175  
 Ser Asp Leu Phe Tyr Trp Pro Arg Arg Ala Gly Lys Leu Gln Gly Ser  
                   180                                  185                                  190  
 His His Lys Pro Leu Ser Lys Thr Ala Asn Gly Leu Ala Gly His Glu  
                   195                                  200                                  205  
 Gly Trp Thr Ile Ala Leu Pro Gly Arg Ala Leu Ala Gln Asn Gly Ser  
                   210                                  215                                  220  
 Leu Gly Glu Gly Ile His Glu Pro Gly Gly Pro Arg Arg Gly Asn Ser  
                   225                                  230                                  235                                  240  
 Thr Asn Arg Arg Val Arg Leu Lys Asn Pro Phe Tyr Pro Leu Thr Gln

309/518

	245	250	255
Glu Ser Tyr Gly Ala Tyr Ala Val Met Cys Leu Ser Val Val Ile Phe			
	260	265	270
Gly Thr Gly Ile Ile Gly Asn Leu Ala Val Met Cys Ile Val Cys His			
	275	280	285
Asn Tyr Tyr Met Arg Ser Ile Ser Asn Ser Leu Leu Ala Asn Leu Ala			
	290	295	300
Phe Trp Asp Phe Leu Ile Ile Phe Phe Cys Leu Pro Leu Val Ile Phe			
	305	310	315
His Glu Leu Thr Lys Lys Trp Leu Leu Glu Asp Phe Ser Cys Lys Ile			
	325	330	335
Val Pro Tyr Ile Glu Val Ala Ser Leu Gly Val Thr Thr Phe Thr Leu			
	340	345	350
Cys Ala Leu Cys Ile Asp Arg Phe Arg Ala Ala Thr Asn Val Gln Met			
	355	360	365
Tyr Tyr Glu Met Ile Glu Asn Cys Ser Ser Thr Thr Ala Lys Leu Ala			
	370	375	380
Val Ile Trp Val Gly Ala Leu Leu Leu Ala Leu Pro Glu Val Val Leu			
	385	390	395
Arg Gln Leu Ser Lys Glu Asp Leu Gly Phe Ser Gly Arg Ala Pro Ala			
	405	410	415
Glu Arg Cys Ile Ile Lys Ile Ser Pro Asp Leu Pro Asp Thr Ile Tyr			
	420	425	430
Val Leu Ala Leu Thr Tyr Asp Ser Ala Arg Leu Trp Trp Tyr Phe Gly			
	435	440	445
Cys Tyr Phe Cys Leu Pro Thr Leu Phe Thr Ile Thr Cys Ser Leu Val			
	450	455	460
Thr Ala Arg Lys Ile Arg Lys Ala Glu Lys Ala Cys Thr Arg Gly Asn			
	465	470	475
			480

310/518

Lys Arg Gln Ile Gln Leu Glu Ser Gln Met Asn Cys Thr Val Val Ala  
 485 490 495  
 Leu Thr Ile Leu Tyr Gly Phe Cys Ile Ile Pro Glu Asn Ile Cys Asn  
 500 505 510  
 Ile Val Thr Ala Tyr Met Ala Thr Gly Val Ser Gln Gln Thr Met Asp  
 515 520 525  
 Leu Leu Asn Ile Ile Ser Gln Phe Leu Leu Phe Phe Lys Ser Cys Val  
 530 535 540  
 Thr Pro Val Leu Leu Phe Cys Leu Cys Lys Pro Phe Ser Arg Ala Phe  
 545 550 555 560  
 Met Glu Cys Cys Cys Cys Cys Cys Glu Glu Cys Ile Gln Lys Ser Ser  
 565 570 575  
 Thr Val Thr Ser Asp Asp Asn Asp Asn Glu Tyr Thr Thr Glu Leu Glu  
 580 585 590  
 Leu Ser Pro Phe Ser Thr Ile Arg Arg Glu Met Ser Thr Phe Ala Ser  
 595 600 605  
 Val Gly Thr His Cys Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val  
 610 615 620  
 Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe  
 625 630 635 640  
 Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr  
 645 650 655  
 Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr  
 660 665 670  
 Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro  
 675 680 685  
 Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly  
 690 695 700  
 Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys

311/518

705	710	715	720
Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile			
	725	730	735
Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His			
	740	745	750
Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp			
	755	760	765
Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile			
	770	775	780
Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro			
785	790	795	800
Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr			
	805	810	815
Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val			
	820	825	830
Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu			
	835	840	845
Leu Tyr Asn			
850			

&lt;210&gt; 117

&lt;211&gt; 719

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 117

Met Arg Trp Leu Trp Pro Leu Ala Val Ser Leu Ala Val Ile Leu Ala			
	5	10	15
Val Gly Leu Ser Arg Val Ser Gly Gly Ala Pro Leu His Leu Gly Arg			

312/518

20	25	30
His Arg Ala Glu Thr Gln Glu Gln Gln Ser Arg Ser Lys Arg Gly Thr		
35	40	45
Glu Asp Glu Glu Ala Lys Gly Val Gln Gln Tyr Val Pro Glu Glu Trp		
50	55	60
Ala Glu Tyr Pro Arg Pro Ile His Pro Ala Gly Leu Gln Pro Thr Lys		
65	70	75
Pro Leu Val Ala Thr Ser Pro Asn Pro Asp Lys Asp Gly Gly Thr Pro		
85	90	95
Asp Ser Gly Gln Glu Leu Arg Gly Asn Leu Thr Gly Ala Pro Gly Gln		
100	105	110
Arg Leu Gln Ile Gln Asn Pro Leu Tyr Pro Val Thr Glu Ser Ser Tyr		
115	120	125
Ser Ala Tyr Ala Ile Met Leu Leu Ala Leu Val Val Phe Ala Val Gly		
130	135	140
Ile Val Gly Asn Leu Ser Val Met Cys Ile Val Trp His Ser Tyr Tyr		
145	150	155
Leu Lys Ser Ala Trp Asn Ser Ile Leu Ala Ser Leu Ala Leu Trp Asp		
165	170	175
Phe Leu Val Leu Phe Phe Cys Leu Pro Ile Val Ile Phe Asn Glu Ile		
180	185	190
Thr Lys Gln Arg Leu Leu Gly Asp Val Ser Cys Arg Ala Val Pro Phe		
195	200	205
Met Glu Val Ser Ser Leu Gly Val Thr Thr Phe Ser Leu Cys Ala Leu		
210	215	220
Gly Ile Asp Arg Phe His Val Ala Thr Ser Thr Leu Pro Lys Val Arg		
225	230	235
Pro Ile Glu Arg Cys Gln Ser Ile Leu Ala Lys Leu Ala Val Ile Trp		
245	250	255

313/518

Val Gly Ser Met Thr Leu Ala Val Pro Glu Leu Leu Leu Trp Gln Leu  
 260 265 270  
 Ala Gln Glu Pro Ala Pro Thr Met Gly Thr Leu Asp Ser Cys Ile Met  
 275 280 285  
 Lys Pro Ser Ala Ser Leu Pro Glu Ser Leu Tyr Ser Leu Val Met Thr  
 290 295 300  
 Tyr Gln Asn Ala Arg Met Trp Trp Tyr Phe Gly Cys Tyr Phe Cys Leu  
 305 310 315 320  
 Pro Ile Leu Phe Thr Val Thr Cys Gln Leu Val Thr Trp Arg Val Arg  
 325 330 335  
 Gly Pro Pro Gly Arg Lys Ser Glu Cys Arg Ala Ser Lys His Glu Gln  
 340 345 350  
 Cys Glu Ser Gln Leu Asn Ser Thr Val Val Gly Leu Thr Val Val Tyr  
 355 360 365  
 Ala Phe Cys Thr Leu Pro Glu Asn Val Cys Asn Ile Val Val Ala Tyr  
 370 375 380  
 Leu Ser Thr Glu Leu Thr Arg Gln Thr Leu Asp Leu Leu Gly Leu Ile  
 385 390 395 400  
 Asn Gln Phe Ser Thr Phe Phe Lys Gly Ala Ile Thr Pro Val Leu Leu  
 405 410 415  
 Leu Cys Ile Cys Arg Pro Leu Gly Gln Ala Phe Leu Asp Cys Cys Cys  
 420 425 430  
 Cys Cys Cys Cys Glu Glu Cys Gly Gly Ala Ser Glu Ala Ser Ala Ala  
 435 440 445  
 Asn Gly Ser Asp Asn Lys Leu Lys Thr Glu Val Ser Ser Ser Ile Tyr  
 450 455 460  
 Phe His Lys Pro Arg Glu Ser Pro Pro Leu Leu Pro Leu Gly Thr Pro  
 465 470 475 480  
 Cys Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu

314/518

485	490	495
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly		
500	505	510
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile		
515	520	525
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr		
530	535	540
Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys		
545	550	555
Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu		
565	570	575
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu		
580	585	590
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly		
595	600	605
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr		
610	615	620
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn		
625	630	635
Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser		
645	650	655
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly		
660	665	670
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu		
675	680	685
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe		
690	695	700
Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn		
705	710	715

315/518

&lt;210&gt; 118

&lt;211&gt; 591

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 118

Met Glu Thr Asn Phe Ser Ile Pro Leu Asn Glu Thr Glu Glu Val Leu

5

10

15

Pro Glu Pro Ala Gly His Thr Val Leu Trp Ile Phe Ser Leu Leu Val

20

25

30

His Gly Val Thr Phe Val Phe Gly Val Leu Gly Asn Gly Leu Val Ile

35

40

45

Trp Val Ala Gly Phe Arg Met Thr Arg Thr Val Asn Thr Ile Cys Tyr

50

55

60

Leu Asn Leu Ala Leu Ala Asp Phe Ser Phe Ser Ala Ile Leu Pro Phe

65

70

75

80

Arg Met Val Ser Val Ala Met Arg Glu Lys Trp Pro Phe Gly Ser Phe

85

90

95

Leu Cys Lys Leu Val His Val Met Ile Asp Ile Asn Leu Phe Val Ser

100

105

110

Val Tyr Leu Ile Thr Ile Ile Ala Leu Asp Arg Cys Ile Cys Val Leu

115

120

125

His Pro Ala Trp Ala Gln Asn His Arg Thr Met Ser Leu Ala Lys Arg

130

135

140

Val Met Thr Gly Leu Trp Ile Phe Thr Ile Val Leu Thr Leu Pro Asn

145

150

155

160

Phe Ile Phe Trp Thr Thr Ile Ser Thr Thr Asn Gly Asp Thr Tyr Cys

165

170

175



316/518

Ile Phe Asn Phe Ala Phe Trp Gly Asp Thr Ala Val Glu Arg Leu Asn			
180	185	190	
Val Phe Ile Thr Met Ala Lys Val Phe Leu Ile Leu His Phe Ile Ile			
195	200	205	
Gly Phe Ser Val Pro Met Ser Ile Ile Thr Val Cys Tyr Gly Ile Ile			
210	215	220	
Ala Ala Lys Ile His Arg Asn His Met Ile Lys Ser Ser Arg Pro Leu			
225	230	235	240
Arg Val Phe Ala Ala Val Val Ala Ser Phe Phe Ile Cys Trp Phe Pro			
245	250	255	
Tyr Glu Leu Ile Gly Ile Leu Met Ala Val Trp Leu Lys Glu Met Leu			
260	265	270	
Leu Asn Gly Lys Tyr Lys Ile Ile Leu Val Leu Ile Asn Pro Thr Ser			
275	280	285	
Ser Leu Ala Phe Phe Asn Ser Cys Leu Asn Pro Ile Leu Tyr Val Phe			
290	295	300	
Met Gly Arg Asn Phe Gln Glu Arg Leu Ile Arg Ser Leu Pro Thr Ser			
305	310	315	320
Leu Glu Arg Ala Leu Thr Glu Val Pro Asp Ser Ala Gln Thr Ser Asn			
325	330	335	
Thr Asp Thr Thr Ser Ala Ser Pro Pro Glu Glu Thr Glu Leu Gln Ala			
340	345	350	
Met Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu			
355	360	365	
Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly			
370	375	380	
Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile			
385	390	395	400
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr			

317/518

	405		410		415
Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys					
	420		425		430
Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu					
	435		440		445
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu					
	450		455		460
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly					
	465		470		475
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr					
	485		490		495
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn					
	500		505		510
Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser					
	515		520		525
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly					
	530		535		540
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu					
	545		550		555
Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe					
	565		570		575
Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn					
	580		585		590

&lt;210&gt; 119

&lt;211&gt; 594

&lt;212&gt; PRT

&lt;213&gt; Human

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&lt;400&gt; 119

Met Asn Gly Val Ser Glu Gly Thr Arg Gly Cys Ser Asp Arg Gln Pro  
                     5                    10                    15  
 Gly Val Leu Thr Arg Asp Arg Ser Cys Ser Arg Lys Met Asn Ser Ser  
                     20                    25                    30  
 Gly Cys Leu Ser Glu Glu Val Gly Ser Leu Arg Pro Leu Thr Val Val  
                     35                    40                    45  
 Ile Leu Ser Ala Ser Ile Val Val Gly Val Leu Gly Asn Gly Leu Val  
                     50                    55                    60  
 Leu Trp Met Thr Val Phe Arg Met Ala Arg Thr Val Ser Thr Val Cys  
                     65                    70                    75                    80  
 Phe Phe His Leu Ala Leu Ala Asp Phe Met Leu Ser Leu Ser Leu Pro  
                     85                    90                    95  
 Ile Ala Met Tyr Tyr Ile Val Ser Arg Gln Trp Leu Leu Gly Glu Trp  
                     100                    105                    110  
 Ala Cys Lys Leu Tyr Ile Thr Phe Val Phe Leu Ser Tyr Phe Ala Ser  
                     115                    120                    125  
 Asn Cys Leu Leu Val Phe Ile Ser Val Asp Arg Cys Ile Ser Val Leu  
                     130                    135                    140  
 Tyr Pro Val Trp Ala Leu Asn His Arg Thr Val Gln Arg Ala Ser Trp  
                     145                    150                    155                    160  
 Leu Ala Phe Gly Val Trp Leu Leu Ala Ala Ala Leu Cys Ser Ala His  
                     165                    170                    175  
 Leu Lys Phe Arg Thr Thr Arg Lys Trp Asn Gly Cys Thr His Cys Tyr  
                     180                    185                    190  
 Leu Ala Phe Asn Ser Asp Asn Glu Thr Ala Gln Ile Trp Ile Glu Gly  
                     195                    200                    205  
 Val Val Glu Gly His Ile Ile Gly Thr Ile Gly His Phe Leu Leu Gly  
                     210                    215                    220

319/518

Phe	Leu	Gly	Pro	Leu	Ala	Ile	Ile	Gly	Thr	Cys	Ala	His	Leu	Ile	Arg
225					230					235					240
Ala	Lys	Leu	Leu	Arg	Glu	Gly	Trp	Val	His	Ala	Asn	Arg	Pro	Lys	Arg
				245						250					255
Leu	Leu	Leu	Val	Leu	Val	Ser	Ala	Phe	Phe	Ile	Phe	Trp	Ser	Pro	Phe
				260						265					270
Asn	Val	Val	Leu	Leu	Val	His	Leu	Trp	Arg	Arg	Val	Met	Leu	Lys	Glu
				275						280					285
Ile	Tyr	His	Pro	Arg	Met	Leu	Leu	Ile	Leu	Gln	Ala	Ser	Phe	Ala	Leu
				290						295					300
Gly	Cys	Val	Asn	Ser	Ser	Leu	Asn	Pro	Phe	Leu	Tyr	Val	Phe	Val	Gly
305						310					315				320
Arg	Asp	Phe	Gln	Glu	Lys	Phe	Phe	Gln	Ser	Leu	Thr	Ser	Ala	Leu	Ala
						325					330				335
Arg	Ala	Phe	Gly	Glu	Glu	Glu	Phe	Leu	Ser	Ser	Cys	Pro	Arg	Gly	Asn
						340					345				350
Ala	Pro	Arg	Glu	Ala	Ser	Lys	Gly	Glu	Glu	Leu	Phe	Thr	Gly	Val	Val
						355					360				365
Pro	Ile	Leu	Val	Glu	Leu	Asp	Gly	Asp	Val	Asn	Gly	His	Lys	Phe	Ser
						370					375				380
Val	Ser	Gly	Glu	Gly	Glu	Gly	Asp	Ala	Thr	Tyr	Gly	Lys	Leu	Thr	Leu
385						390					395				400
Lys	Phe	Ile	Cys	Thr	Thr	Gly	Lys	Leu	Pro	Val	Pro	Trp	Pro	Thr	Leu
						405					410				415
Val	Thr	Thr	Leu	Cys	Tyr	Gly	Val	Gln	Cys	Phe	Ser	Arg	Tyr	Pro	Asp
						420					425				430
His	Met	Lys	Arg	His	Asp	Phe	Phe	Lys	Ser	Ala	Met	Pro	Glu	Gly	Tyr
						435					440				445
Val	Gln	Glu	Arg	Thr	Ile	Phe	Phe	Lys	Asp	Asp	Gly	Asn	Tyr	Lys	Thr

320/518

450                      455                      460  
 Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu  
 465                      470                      475                      480  
 Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys  
                          485                      490                      495  
 Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys  
                          500                      505                      510  
 Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu  
                          515                      520                      525  
 Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile  
                          530                      535                      540  
 Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln  
 545                      550                      555                      560  
 Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu  
                          565                      570                      575  
 Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu  
                          580                      585                      590  
 Tyr Asn

&lt;210&gt; 120

&lt;211&gt; 1459

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 120

Met Met Phe Arg Ser Asp Arg Met Trp Ser Cys His Trp Lys Trp Lys  
                          5                      10                      15  
 Pro Ser Pro Leu Leu Phe Leu Phe Ala Leu Tyr Ile Met Cys Val Pro  
                          20                      25                      30

321/518

His Ser Val Trp Gly Cys Ala Asn Cys Arg Val Val Leu Ser Asn Pro  
 35 40 45  
 Ser Gly Thr Phe Thr Ser Pro Cys Tyr Pro Asn Asp Tyr Pro Asn Ser  
 50 55 60  
 Gln Ala Cys Met Trp Thr Leu Arg Ala Pro Thr Gly Tyr Ile Ile Gln  
 65 70 75 80  
 Ile Thr Phe Asn Asp Phe Asp Ile Glu Glu Ala Pro Asn Cys Ile Tyr  
 85 90 95  
 Asp Ser Leu Ser Leu Asp Asn Gly Glu Ser Gln Thr Lys Phe Cys Gly  
 100 105 110  
 Ala Thr Ala Lys Gly Leu Ser Phe Asn Ser Ser Ala Asn Glu Met His  
 115 120 125  
 Val Ser Phe Ser Ser Asp Phe Ser Ile Gln Lys Lys Gly Phe Asn Ala  
 130 135 140  
 Ser Tyr Ile Arg Val Ala Val Ser Leu Arg Asn Gln Lys Val Ile Leu  
 145 150 155 160  
 Pro Gln Thr Ser Asp Ala Tyr Gln Val Ser Val Ala Lys Ser Ile Ser  
 165 170 175  
 Ile Pro Glu Leu Ser Ala Phe Thr Leu Cys Phe Glu Ala Thr Lys Val  
 180 185 190  
 Gly His Glu Asp Ser Asp Trp Thr Ala Phe Ser Tyr Ser Asn Ala Ser  
 195 200 205  
 Phe Thr Gln Leu Leu Ser Phe Gly Lys Ala Lys Ser Gly Tyr Phe Leu  
 210 215 220  
 Ser Ile Ser Asp Ser Lys Cys Leu Leu Asn Asn Ala Leu Pro Val Lys  
 225 230 235 240  
 Glu Lys Glu Asp Ile Phe Ala Glu Ser Phe Glu Gln Leu Cys Leu Val  
 245 250 255  
 Trp Asn Asn Ser Leu Gly Ser Ile Gly Val Asn Phe Lys Arg Asn Tyr

322/518

260	265	270
Glu Thr Val Pro Cys Asp Ser Thr Ile Ser Lys Val Ile Pro Gly Asn		
275	280	285
Gly Lys Leu Leu Leu Gly Ser Asn Gln Asn Glu Ile Val Ser Leu Lys		
290	295	300
Gly Asp Ile Tyr Asn Phe Arg Leu Trp Asn Phe Thr Met Asn Ala Lys		
305	310	315
Ile Leu Ser Asn Leu Ser Cys Asn Val Lys Gly Asn Val Val Asp Trp		
325	330	335
Gln Asn Asp Phe Trp Asn Ile Pro Asn Leu Ala Leu Lys Ala Glu Ser		
340	345	350
Asn Leu Ser Cys Gly Ser Tyr Leu Ile Pro Leu Pro Ala Ala Glu Leu		
355	360	365
Ala Ser Cys Ala Asp Leu Gly Thr Leu Cys Gln Ala Thr Val Asn Ser		
370	375	380
Pro Ser Thr Thr Pro Pro Thr Val Thr Thr Asn Met Pro Val Thr Asn		
385	390	395
Arg Ile Asp Lys Gln Arg Asn Asp Gly Ile Ile Tyr Arg Ile Ser Val		
405	410	415
Val Ile Gln Asn Ile Leu Arg His Pro Glu Val Lys Val Gln Ser Lys		
420	425	430
Val Ala Glu Trp Leu Asn Ser Thr Phe Gln Asn Trp Asn Tyr Thr Val		
435	440	445
Tyr Val Val Asn Ile Ser Phe His Leu Ser Ala Gly Glu Asp Lys Ile		
450	455	460
Lys Val Lys Arg Ser Leu Glu Asp Glu Pro Arg Leu Val Leu Trp Ala		
465	470	475
Leu Leu Val Tyr Asn Ala Thr Asn Asn Thr Asn Leu Glu Gly Lys Ile		
485	490	495

323/518

Ile Gln Gln Lys Leu Leu Lys Asn Asn Glu Ser Leu Asp Glu Gly Leu  
 500 505 510  
 Arg Leu His Thr Val Asn Val Arg Gln Leu Gly His Cys Leu Ala Met  
 515 520 525  
 Glu Glu Pro Lys Gly Tyr Tyr Trp Pro Ser Ile Gln Pro Ser Glu Tyr  
 530 535 540  
 Val Leu Pro Cys Pro Asp Lys Pro Gly Phe Ser Ala Ser Arg Ile Cys  
 545 550 555 560  
 Phe Tyr Asn Ala Thr Asn Pro Leu Val Thr Tyr Trp Gly Pro Val Asp  
 565 570 575  
 Ile Ser Asn Cys Leu Lys Glu Ala Asn Glu Val Ala Asn Gln Ile Leu  
 580 585 590  
 Asn Leu Thr Ala Asp Gly Gln Asn Leu Thr Ser Ala Asn Ile Thr Asn  
 595 600 605  
 Ile Val Glu Gln Val Lys Arg Ile Val Asn Lys Glu Glu Asn Ile Asp  
 610 615 620  
 Ile Thr Leu Gly Ser Thr Leu Met Asn Ile Phe Ser Asn Ile Leu Ser  
 625 630 635 640  
 Ser Ser Asp Ser Asp Leu Leu Glu Ser Ser Ser Glu Ala Leu Lys Thr  
 645 650 655  
 Ile Asp Glu Leu Ala Phe Lys Ile Asp Leu Asn Ser Thr Ser His Val  
 660 665 670  
 Asn Ile Thr Thr Arg Asn Leu Ala Leu Ser Val Ser Ser Leu Leu Pro  
 675 680 685  
 Gly Thr Asn Ala Ile Ser Asn Phe Ser Ile Gly Leu Pro Ser Asn Asn  
 690 695 700  
 Glu Ser Tyr Phe Gln Met Asp Phe Glu Ser Gly Gln Val Asp Pro Leu  
 705 710 715 720  
 Ala Ser Val Ile Leu Pro Pro Asn Leu Leu Glu Asn Leu Ser Pro Glu



324/518

725	730	735	
Asp Ser Val Leu Val Arg Arg Ala Gln Phe Thr Phe Phe Asn Lys Thr			
740	745	750	
Gly Leu Phe Gln Asp Val Gly Pro Gln Arg Lys Thr Leu Val Ser Tyr			
755	760	765	
Val Met Ala Cys Ser Ile Gly Asn Ile Thr Ile Gln Asn Leu Lys Asp			
770	775	780	
Pro Val Gln Ile Lys Ile Lys His Thr Arg Thr Gln Glu Val His His			
785	790	795	800
Pro Ile Cys Ala Phe Trp Asp Leu Asn Lys Asn Lys Ser Phe Gly Gly			
805	810	815	
Trp Asn Thr Ser Gly Cys Val Ala His Arg Asp Ser Asp Ala Ser Glu			
820	825	830	
Thr Val Cys Leu Cys Asn His Phe Thr His Phe Gly Val Leu Met Asp			
835	840	845	
Leu Pro Arg Ser Ala Ser Gln Leu Asp Ala Arg Asn Thr Lys Val Leu			
850	855	860	
Thr Phe Ile Ser Tyr Ile Gly Cys Gly Ile Ser Ala Ile Phe Ser Ala			
865	870	875	880
Ala Thr Leu Leu Thr Tyr Val Ala Phe Glu Lys Leu Arg Arg Asp Tyr			
885	890	895	
Pro Ser Lys Ile Leu Met Asn Leu Ser Thr Ala Leu Leu Phe Leu Asn			
900	905	910	
Leu Leu Phe Leu Leu Asp Gly Trp Ile Thr Ser Phe Asn Val Asp Gly			
915	920	925	
Leu Cys Ile Ala Val Ala Val Leu Leu His Phe Phe Leu Leu Ala Thr			
930	935	940	
Phe Thr Trp Met Gly Leu Glu Ala Ile His Met Tyr Ile Ala Leu Val			
945	950	955	960

325/518

Lys Val Phe Asn Thr Tyr Ile Arg Arg Tyr Ile Leu Lys Phe Cys Ile  
965 970 975  
Ile Gly Trp Gly Leu Pro Ala Leu Val Val Ser Val Val Leu Ala Ser  
980 985 990  
Arg Asn Asn Asn Glu Val Tyr Gly Lys Glu Ser Tyr Gly Lys Glu Lys  
995 1000 1005  
Gly Asp Glu Phe Cys Trp Ile Gln Asp Pro Val Ile Phe Tyr Val Thr  
1010 1015 1020  
Cys Ala Gly Tyr Phe Gly Val Met Phe Phe Leu Asn Ile Ala Met Phe  
1025 1030 1035 1040  
Ile Val Val Met Val Gln Ile Cys Gly Arg Asn Gly Lys Arg Ser Asn  
1045 1050 1055  
Arg Thr Leu Arg Glu Glu Val Leu Arg Asn Leu Arg Ser Val Val Ser  
1060 1065 1070  
Leu Thr Phe Leu Leu Gly Met Thr Trp Gly Phe Ala Phe Phe Ala Trp  
1075 1080 1085  
Gly Pro Leu Asn Ile Pro Phe Met Tyr Leu Phe Ser Ile Phe Asn Ser  
1090 1095 1100  
Leu Gln Gly Leu Phe Ile Phe Ile Phe His Cys Ala Met Lys Glu Asn  
1105 1110 1115 1120  
Val Gln Lys Gln Trp Arg Arg His Leu Cys Cys Gly Arg Phe Arg Leu  
1125 1130 1135  
Ala Asp Asn Ser Asp Trp Ser Lys Thr Ala Thr Asn Ile Ile Lys Lys  
1140 1145 1150  
Ser Ser Asp Asn Leu Gly Lys Ser Leu Ser Ser Ser Ser Ile Gly Ser  
1155 1160 1165  
Asn Ser Thr Tyr Leu Thr Ser Lys Ser Lys Ser Ser Ser Thr Thr Tyr  
1170 1175 1180  
Phe Lys Arg Asn Ser His Thr Asp Asn Val Ser Tyr Glu His Ser Phe

326/518

1185	1190	1195	1200
Asn Lys Ser Gly Ser Leu Arg Gln Cys Phe His Gly Gln Val Leu Val			
1205	1210	1215	
Lys Thr Gly Pro Cys Ser Ser Lys Gly Glu Glu Leu Phe Thr Gly Val			
1220	1225	1230	
Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe			
1235	1240	1245	
Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr			
1250	1255	1260	
Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr			
1265	1270	1275	1280
Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro			
1285	1290	1295	
Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly			
1300	1305	1310	
Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys			
1315	1320	1325	
Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile			
1330	1335	1340	
Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His			
1345	1350	1355	1360
Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp			
1365	1370	1375	
Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile			
1380	1385	1390	
Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro			
1395	1400	1405	
Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr			
1410	1415	1420	

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Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val  
 1425                      1430                      1435                      1440  
 Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu  
                          1445                      1450                      1455  
 Leu Tyr Asn

&lt;210&gt; 121

&lt;211&gt; 637

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 121

Met Ala Gln Arg Gln Pro His Ser Pro Asn Gln Thr Leu Ile Ser Ile  
                          5                      10                      15  
 Thr Asn Asp Thr Glu Ser Ser Ser Ser Val Val Ser Asn Asp Asn Thr  
                          20                      25                      30  
 Asn Lys Gly Trp Ser Gly Asp Asn Ser Pro Gly Ile Glu Ala Leu Cys  
                          35                      40                      45  
 Ala Ile Tyr Ile Thr Tyr Ala Val Ile Ile Ser Val Gly Ile Leu Gly  
                          50                      55                      60  
 Asn Ala Ile Leu Ile Lys Val Phe Phe Lys Thr Lys Ser Met Gln Thr  
                          65                      70                      75                      80  
 Val Pro Asn Ile Phe Ile Thr Ser Leu Ala Phe Gly Asp Leu Leu Leu  
                          85                      90                      95  
 Leu Leu Thr Cys Val Pro Val Asp Ala Thr His Tyr Leu Ala Glu Gly  
                          100                      105                      110  
 Trp Leu Phe Gly Arg Ile Gly Cys Lys Val Leu Ser Phe Ile Arg Leu  
                          115                      120                      125  
 Thr Ser Val Gly Val Ser Val Phe Thr Leu Thr Ile Leu Ser Ala Asp

328/518

130	135	140	
Arg Tyr Lys Ala Val	Val Lys Pro Leu Glu Arg	Gln Pro Ser Asn Ala	
145	150	155	160
Ile Leu Lys Thr Cys	Val Lys Ala Gly Cys	Val Trp Ile Val Ser Met	
	165	170	175
Ile Phe Ala Leu Pro	Glu Ala Ile Phe Ser Asn	Val Tyr Thr Phe Arg	
	180	185	190
Asp Pro Asn Lys Asn	Met Thr Phe Glu Ser Cys	Thr Ser Tyr Pro Val	
	195	200	205
Ser Lys Lys Leu Leu	Gln Glu Ile His Ser Leu	Leu Cys Phe Leu Val	
	210	215	220
Phe Tyr Ile Ile Pro	Leu Ser Ile Ile Ser Val	Tyr Tyr Ser Leu Ile	
	225	230	235
Ala Arg Thr Leu Tyr	Lys Ser Thr Leu Asn Ile	Pro Thr Glu Glu Gln	
	245	250	255
Ser His Ala Arg Lys	Gln Ile Glu Ser Arg Lys	Arg Ile Ala Arg Thr	
	260	265	270
Val Leu Val Leu Val	Ala Leu Phe Ala Leu Cys	Trp Leu Pro Asn His	
	275	280	285
Leu Leu Tyr Leu Tyr	His Ser Phe Thr Ser Gln	Thr Tyr Val Asp Pro	
	290	295	300
Ser Ala Met His Phe	Ile Phe Thr Ile Phe Ser	Arg Val Leu Ala Phe	
	305	310	315
Ser Asn Ser Cys Val	Asn Pro Phe Ala Leu Tyr	Trp Leu Ser Lys Ser	
	325	330	335
Phe Gln Lys His Phe	Lys Ala Gln Leu Phe Cys	Cys Lys Ala Glu Arg	
	340	345	350
Pro Glu Pro Pro Val	Ala Asp Thr Ser Leu Thr	Thr Leu Ala Val Met	
	355	360	365

329/518

Gly Thr Val Pro Gly Thr Gly Ser Ile Gln Met Ser Glu Ile Ser Val  
 370 375 380  
 Thr Ser Phe Thr Gly Cys Ser Val Lys Gln Ala Glu Asp Arg Phe Ala  
 385 390 395 400  
 Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu  
 405 410 415  
 Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly  
 420 425 430  
 Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr  
 435 440 445  
 Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys  
 450 455 460  
 Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His  
 465 470 475 480  
 Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr  
 485 490 495  
 Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys  
 500 505 510  
 Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp  
 515 520 525  
 Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr  
 530 535 540  
 Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile  
 545 550 555 560  
 Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln  
 565 570 575  
 Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val  
 580 585 590  
 Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys

605

620

635

<213> Human

15

30

45

60

80

95

110

125

Leu Ser Phe Glu Arg Tyr Ile Ala Ile Cys His Pro Phe Arg Tyr Lys

331/518

130	135	140	
Ala Val Ser Gly Pro Cys Gln Val Lys Leu Leu Ile Gly Phe Val Trp			
145	150	155	160
Val Thr Ser Ala Leu Val Ala Leu Pro Leu Leu Phe Ala Met Gly Thr			
	165	170	175
Glu Tyr Pro Leu Val Asn Val Pro Ser His Arg Gly Leu Thr Cys Asn			
	180	185	190
Arg Ser Ser Thr Arg His His Glu Gln Pro Glu Thr Ser Asn Met Ser			
	195	200	205
Ile Cys Thr Asn Leu Ser Ser Arg Trp Thr Val Phe Gln Ser Ser Ile			
	210	215	220
Phe Gly Ala Phe Val Val Tyr Leu Val Val Leu Leu Ser Val Ala Phe			
225	230	235	240
Met Cys Trp Asn Met Met Gln Val Leu Met Lys Ser Gln Lys Gly Ser			
	245	250	255
Leu Ala Gly Gly Thr Arg Pro Pro Gln Leu Arg Lys Ser Glu Ser Glu			
	260	265	270
Glu Ser Arg Thr Ala Arg Arg Gln Thr Ile Ile Phe Leu Arg Leu Ile			
	275	280	285
Val Val Thr Leu Ala Val Cys Trp Met Pro Asn Gln Ile Arg Arg Ile			
	290	295	300
Met Ala Ala Ala Lys Pro Lys His Asp Trp Thr Arg Ser Tyr Phe Arg			
305	310	315	320
Ala Tyr Met Ile Leu Leu Pro Phe Ser Glu Thr Phe Phe Tyr Leu Ser			
	325	330	335
Ser Val Ile Asn Pro Leu Leu Tyr Thr Val Ser Ser Gln Gln Phe Arg			
	340	345	350
Arg Val Phe Val Gln Val Leu Cys Cys Arg Leu Ser Leu Gln His Ala			
	355	360	365



332/518

Asn His Glu Lys Arg Leu Arg Val His Ala His Ser Thr Thr Asp Ser  
 370 375 380  
 Ala Arg Phe Val Gln Arg Pro Leu Leu Phe Ala Ser Arg Arg Gln Ser  
 385 390 395 400  
 Ser Ala Arg Arg Thr Glu Lys Ile Phe Leu Ser Thr Phe Gln Ser Glu  
 405 410 415  
 Ala Glu Pro Gln Ser Lys Ser Gln Ser Leu Ser Leu Glu Ser Leu Glu  
 420 425 430  
 Pro Asn Ser Gly Ala Lys Pro Ala Asn Ser Ala Ala Glu Asn Gly Phe  
 435 440 445  
 Gln Glu His Glu Val Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val  
 450 455 460  
 Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe  
 465 470 475 480  
 Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr  
 485 490 495  
 Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr  
 500 505 510  
 Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro  
 515 520 525  
 Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly  
 530 535 540  
 Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys  
 545 550 555 560  
 Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile  
 565 570 575  
 Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His  
 580 585 590  
 Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp

333/518

595                      600                      605  
 Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile  
 610                      615                      620  
 Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro  
 625                      630                      635                      640  
 Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr  
 645                      650                      655  
 Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val  
 660                      665                      670  
 Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu  
 675                      680                      685  
 Leu Tyr Asn  
 690

<210> 123  
 <211> 661  
 <212> PRT  
 <213> Human

<400> 123  
 Met Val Pro His Leu Leu Leu Leu Cys Leu Leu Pro Leu Val Arg Ala  
 5                      10                      15  
 Thr Glu Pro His Glu Gly Arg Ala Asp Glu Gln Ser Ala Glu Ala Ala  
 20                      25                      30  
 Leu Ala Val Pro Asn Ala Ser His Phe Phe Ser Trp Asn Asn Tyr Thr  
 35                      40                      45  
 Phe Ser Asp Trp Gln Asn Phe Val Gly Arg Arg Arg Tyr Gly Ala Glu  
 50                      55                      60  
 Ser Gln Asn Pro Thr Val Lys Ala Leu Leu Ile Val Ala Tyr Ser Phe

334/518

65	70	75	80
Ile Ile Val Phe Ser Leu Phe Gly Asn Val Leu Val Cys His Val Ile			
	85	90	95
Phe Lys Asn Gln Arg Met His Ser Ala Thr Ser Leu Phe Ile Val Asn			
	100	105	110
Leu Ala Val Ala Asp Ile Met Ile Thr Leu Leu Asn Thr Pro Phe Thr			
	115	120	125
Leu Val Arg Phe Val Asn Ser Thr Trp Ile Phe Gly Lys Gly Met Cys			
	130	135	140
His Val Ser Arg Phe Ala Gln Tyr Cys Ser Leu His Val Ser Ala Leu			
145	150	155	160
Thr Leu Thr Ala Ile Ala Val Asp Arg His Gln Val Ile Met His Pro			
	165	170	175
Leu Lys Pro Arg Ile Ser Ile Thr Lys Gly Val Ile Tyr Ile Ala Val			
	180	185	190
Ile Trp Thr Met Ala Thr Phe Phe Ser Leu Pro His Ala Ile Cys Gln			
	195	200	205
Lys Leu Phe Thr Phe Lys Tyr Ser Glu Asp Ile Val Arg Ser Leu Cys			
	210	215	220
Leu Pro Asp Phe Pro Glu Pro Ala Asp Leu Phe Trp Lys Tyr Leu Asp			
225	230	235	240
Leu Ala Thr Phe Ile Leu Leu Tyr Ile Leu Pro Leu Leu Ile Ile Ser			
	245	250	255
Val Ala Tyr Ala Arg Val Ala Lys Lys Leu Trp Leu Cys Asn Met Ile			
	260	265	270
Gly Asp Val Thr Thr Glu Gln Tyr Phe Ala Leu Arg Arg Lys Lys Lys			
	275	280	285
Lys Thr Ile Lys Met Leu Met Leu Val Val Val Leu Phe Ala Leu Cys			
	290	295	300

335/518

Trp Phe Pro Leu Asn Cys Tyr Val Leu Leu Leu Ser Ser Lys Val Ile  
 305                      310                      315                      320  
 Arg Thr Asn Asn Ala Leu Tyr Phe Ala Phe His Trp Phe Ala Met Ser  
                          325                      330                      335  
 Ser Thr Cys Tyr Asn Pro Phe Ile Tyr Cys Trp Leu Asn Glu Asn Phe  
                          340                      345                      350  
 Arg Ile Glu Leu Lys Ala Leu Leu Ser Met Cys Gln Arg Pro Pro Lys  
                          355                      360                      365  
 Pro Gln Glu Asp Arg Pro Pro Ser Pro Val Pro Ser Phe Arg Val Ala  
                          370                      375                      380  
 Trp Thr Glu Lys Asn Asp Gly Gln Arg Ala Pro Leu Ala Asn Asn Leu  
 385                      390                      395                      400  
 Leu Pro Thr Ser Gln Leu Gln Ser Gly Lys Thr Asp Leu Ser Ser Val  
                          405                      410                      415  
 Glu Pro Ile Val Thr Met Ser Ala Ser Lys Gly Glu Glu Leu Phe Thr  
                          420                      425                      430  
 Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His  
                          435                      440                      445  
 Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys  
                          450                      455                      460  
 Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp  
 465                      470                      475                      480  
 Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg  
                          485                      490                      495  
 Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro  
                          500                      505                      510  
 Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn  
                          515                      520                      525  
 Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn

336/518

530                      535                      540  
 Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu  
 545                      550                      555                      560  
 Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met  
                     565                      570                      575  
 Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His  
                     580                      585                      590  
 Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn  
                     595                      600                      605  
 Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu  
                     610                      615                      620  
 Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His  
 625                      630                      635                      640  
 Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met  
                     645                      650                      655  
 Asp Glu Leu Tyr Asn  
                     660

&lt;210&gt; 124

&lt;211&gt; 634

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 124

Met Trp Asn Ser Ser Asp Ala Asn Phe Ser Cys Tyr His Glu Ser Val  
                     5                      10                      15  
 Leu Gly Tyr Arg Tyr Val Ala Val Ser Trp Gly Val Val Val Ala Val  
                     20                      25                      30  
 Thr Gly Thr Val Gly Asn Val Leu Thr Leu Leu Ala Leu Ala Ile Gln

337/518

35	40	45
Pro Lys Leu Arg Thr Arg Phe Asn Leu Leu Ile Ala Asn Leu Thr Leu		
50	55	60
Ala Asp Leu Leu Tyr Cys Thr Leu Leu Gln Pro Phe Ser Val Asp Thr		
65	70	75
Tyr Leu His Leu His Trp Arg Thr Gly Ala Thr Phe Cys Arg Val Phe		
85	90	95
Gly Leu Leu Leu Phe Ala Ser Asn Ser Val Ser Ile Leu Thr Leu Cys		
100	105	110
Leu Ile Ala Leu Gly Arg Tyr Leu Leu Ile Ala His Pro Lys Leu Phe		
115	120	125
Pro Gln Val Phe Ser Ala Lys Gly Ile Val Leu Ala Leu Val Ser Thr		
130	135	140
Trp Val Val Gly Val Ala Ser Phe Ala Pro Leu Trp Pro Ile Tyr Ile		
145	150	155
Leu Val Pro Val Val Cys Thr Cys Ser Phe Asp Arg Ile Arg Gly Arg		
165	170	175
Pro Tyr Thr Thr Ile Leu Met Gly Ile Tyr Phe Val Leu Gly Leu Ser		
180	185	190
Ser Val Gly Ile Phe Tyr Cys Leu Ile His Arg Gln Val Lys Arg Ala		
195	200	205
Ala Gln Ala Leu Asp Gln Tyr Lys Leu Arg Gln Ala Ser Ile His Ser		
210	215	220
Asn His Val Ala Arg Thr Asp Glu Ala Met Pro Gly Arg Phe Gln Glu		
225	230	235
Leu Asp Ser Arg Leu Ala Ser Gly Gly Pro Ser Glu Gly Ile Ser Ser		
245	250	255
Glu Pro Val Ser Ala Ala Thr Thr Gln Thr Leu Glu Gly Asp Ser Ser		
260	265	270

338/518

Glu Val Gly Asp Gln Ile Asn Ser Lys Arg Ala Lys Gln Met Ala Glu  
 275 280 285  
 Lys Ser Pro Pro Glu Ala Ser Ala Lys Ala Gln Pro Ile Lys Gly Ala  
 290 295 300  
 Arg Arg Ala Pro Asp Ser Ser Ser Glu Phe Gly Lys Val Thr Arg Met  
 305 310 315 320  
 Cys Phe Ala Val Phe Leu Cys Phe Ala Leu Ser Tyr Ile Pro Phe Leu  
 325 330 335  
 Leu Leu Asn Ile Leu Asp Ala Arg Val Gln Ala Pro Arg Val Val His  
 340 345 350  
 Met Leu Ala Ala Asn Leu Thr Trp Leu Asn Gly Cys Ile Asn Pro Val  
 355 360 365  
 Leu Tyr Ala Ala Met Asn Arg Gln Phe Arg Gln Ala Tyr Gly Ser Ile  
 370 375 380  
 Leu Lys Arg Gly Pro Arg Ser Phe His Arg Leu His Ala Ser Lys Gly  
 385 390 395 400  
 Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly  
 405 410 415  
 Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp  
 420 425 430  
 Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys  
 435 440 445  
 Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val  
 450 455 460  
 Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe  
 465 470 475 480  
 Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe  
 485 490 495  
 Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly

339/518

500	505	510	
Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu			
515	520	525	
Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His			
530	535	540	
Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn			
545	550	555	560
Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp			
565	570	575	
His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro			
580	585	590	
Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn			
595	600	605	
Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly			
610	615	620	
Ile Thr His Gly Met Asp Glu Leu Tyr Asn			
625	630		

&lt;210&gt; 125

&lt;211&gt; 587

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 125

Met Asn Ser Thr Leu Asp Gly Asn Gln Ser Ser His Pro Phe Cys Leu		
5	10	15
Leu Ala Phe Gly Tyr Leu Glu Thr Val Asn Phe Cys Leu Leu Glu Val		
20	25	30
Leu Ile Ile Val Phe Leu Thr Val Leu Ile Ile Ser Gly Asn Ile Ile		



340/518

35	40	45	
Val Ile Phe Val Phe His Cys Ala Pro Leu Leu Asn His His Thr Thr			
50	55	60	
Ser Tyr Phe Ile Gln Thr Met Ala Tyr Ala Asp Leu Phe Val Gly Val			
65	70	75	80
Ser Cys Val Val Pro Ser Leu Ser Leu Leu His His Pro Leu Pro Val			
85	90	95	
Glu Glu Ser Leu Thr Cys Gln Ile Phe Gly Phe Val Val Ser Val Leu			
100	105	110	
Lys Ser Val Ser Met Ala Ser Leu Ala Cys Ile Ser Ile Asp Arg Tyr			
115	120	125	
Ile Ala Ile Thr Lys Pro Leu Thr Tyr Asn Thr Leu Val Thr Pro Trp			
130	135	140	
Arg Leu Arg Leu Cys Ile Phe Leu Ile Trp Leu Tyr Ser Thr Leu Val			
145	150	155	160
Phe Leu Pro Ser Phe Phe His Trp Gly Lys Pro Gly Tyr His Gly Asp			
165	170	175	
Val Phe Gln Trp Cys Ala Glu Ser Trp His Thr Asp Ser Tyr Phe Thr			
180	185	190	
Leu Phe Ile Val Met Met Leu Tyr Ala Pro Ala Ala Leu Ile Val Cys			
195	200	205	
Phe Thr Tyr Phe Asn Ile Phe Arg Ile Cys Gln Gln His Thr Lys Asp			
210	215	220	
Ile Ser Glu Arg Gln Ala Arg Phe Ser Ser Gln Ser Gly Glu Thr Gly			
225	230	235	240
Glu Val Gln Ala Cys Pro Asp Lys Arg Tyr Ala Met Val Leu Phe Arg			
245	250	255	
Ile Thr Ser Val Phe Tyr Ile Leu Trp Leu Pro Tyr Ile Ile Tyr Phe			
260	265	270	

341/518

Leu Leu Glu Ser Ser Thr Gly His Ser Asn Arg Phe Ala Ser Phe Leu  
 275 280 285  
 Thr Thr Trp Leu Ala Ile Ser Asn Ser Phe Cys Asn Cys Val Ile Tyr  
 290 295 300  
 Ser Leu Ser Asn Ser Val Phe Gln Arg Gly Leu Lys Arg Leu Ser Gly  
 305 310 315 320  
 Ala Met Cys Thr Ser Cys Ala Ser Gln Thr Thr Ala Asn Asp Pro Tyr  
 325 330 335  
 Thr Val Arg Ser Lys Gly Pro Leu Asn Gly Cys His Ile Ala Ser Lys  
 340 345 350  
 Gly Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp  
 355 360 365  
 Gly Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly  
 370 375 380  
 Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly  
 385 390 395 400  
 Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly  
 405 410 415  
 Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe  
 420 425 430  
 Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe  
 435 440 445  
 Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu  
 450 455 460  
 Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys  
 465 470 475 480  
 Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser  
 485 490 495  
 His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val

342/518

500	505	510
Asn Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala		
515	520	525
Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu		
530	535	540
Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro		
545	550	555
Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala		
565	570	575
Gly Ile Thr His Gly Met Asp Glu Leu Tyr Asn		
580	585	

&lt;210&gt; 126

&lt;211&gt; 1189

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 126

Met Pro Gly Pro Leu Gly Leu Leu Cys Phe Leu Ala Leu Gly Leu Leu		
5	10	15
Gly Ser Ala Gly Pro Ser Gly Ala Ala Pro Pro Leu Cys Ala Ala Pro		
20	25	30
Cys Ser Cys Asp Gly Asp Arg Arg Val Asp Cys Ser Gly Lys Gly Leu		
35	40	45
Thr Ala Val Pro Glu Gly Leu Ser Ala Phe Thr Gln Ala Leu Asp Ile		
50	55	60
Ser Met Asn Asn Ile Thr Gln Leu Pro Glu Asp Ala Phe Lys Asn Phe		
65	70	75
Pro Phe Leu Glu Glu Leu Gln Leu Ala Gly Asn Asp Leu Ser Phe Ile		

343/518

	85	90	95
His Pro Lys Ala Leu Ser Gly Leu Lys Glu Leu Lys Val Leu Thr Leu			
	100	105	110
Gln Asn Asn Gln Leu Lys Thr Val Pro Ser Glu Ala Ile Arg Gly Leu			
	115	120	125
Ser Ala Leu Gln Ser Leu Arg Leu Asp Ala Asn His Ile Thr Ser Val			
	130	135	140
Pro Glu Asp Ser Phe Glu Gly Leu Val Gln Leu Arg His Leu Trp Leu			
	145	150	155
Asp Asp Asn Ser Leu Thr Glu Val Pro Val His Pro Leu Ser Asn Leu			
	165	170	175
Pro Thr Leu Gln Ala Leu Thr Leu Ala Leu Asn Lys Ile Ser Ser Ile			
	180	185	190
Pro Asp Phe Ala Phe Thr Asn Leu Ser Ser Leu Val Val Leu His Leu			
	195	200	205
His Asn Asn Lys Ile Arg Ser Leu Ser Gln His Cys Phe Asp Gly Leu			
	210	215	220
Asp Asn Leu Glu Thr Leu Asp Leu Asn Tyr Asn Asn Leu Gly Glu Phe			
	225	230	235
Pro Gln Ala Ile Lys Ala Leu Pro Ser Leu Lys Glu Leu Gly Phe His			
	245	250	255
Ser Asn Ser Ile Ser Val Ile Pro Asp Gly Ala Phe Asp Gly Asn Pro			
	260	265	270
Leu Leu Arg Thr Ile His Leu Tyr Asp Asn Pro Leu Ser Phe Val Gly			
	275	280	285
Asn Ser Ala Phe His Asn Leu Ser Asp Leu His Ser Leu Val Ile Arg			
	290	295	300
Gly Ala Ser Met Val Gln Gln Phe Pro Asn Leu Thr Gly Thr Val His			
	305	310	315
			320

344/518

Leu Glu Ser Leu Thr Leu Thr Gly Thr Lys Ile Ser Ser Ile Pro Asn

325

330

335

Asn Leu Cys Gln Glu Gln Lys Met Leu Arg Thr Leu Asp Leu Ser Tyr

340

345

350

Asn Asn Ile Arg Asp Leu Pro Ser Phe Asn Gly Cys His Ala Leu Glu

355

360

365

Glu Ile Ser Leu Gln Arg Asn Gln Ile Tyr Gln Ile Lys Glu Gly Thr

370

375

380

Phe Gln Gly Leu Ile Ser Leu Arg Ile Leu Asp Leu Ser Arg Asn Leu

385

390

395

400

Ile His Glu Ile His Ser Arg Ala Phe Ala Thr Leu Gly Pro Ile Thr

405

410

415

Asn Leu Asp Val Ser Phe Asn Glu Leu Thr Ser Phe Pro Thr Glu Gly

420

425

430

Leu Asn Gly Leu Asn Gln Leu Lys Leu Val Gly Asn Phe Lys Leu Lys

435

440

445

Glu Ala Leu Ala Ala Lys Asp Phe Val Asn Leu Arg Ser Leu Ser Val

450

455

460

Pro Tyr Ala Tyr Gln Cys Cys Ala Phe Trp Gly Cys Asp Ser Tyr Ala

465

470

475

480

Asn Leu Asn Thr Glu Asp Asn Ser Leu Gln Asp His Ser Val Ala Gln

485

490

495

Glu Lys Gly Thr Ala Asp Ala Ala Asn Val Thr Ser Thr Leu Glu Asn

500

505

510

Glu Glu His Ser Gln Ile Ile Ile His Cys Thr Pro Ser Thr Gly Ala

515

520

525

Phe Lys Pro Cys Glu Tyr Leu Leu Gly Ser Trp Met Ile Arg Leu Thr

530

535

540

Val Trp Phe Ile Phe Leu Val Ala Leu Phe Phe Asn Leu Leu Val Ile

345/518

545	550	555	560
Leu Thr Thr Phe Ala Ser Cys Thr Ser Leu Pro Ser Ser Lys Leu Phe			
	565	570	575
Ile Gly Leu Ile Ser Val Ser Asn Leu Phe Met Gly Ile Tyr Thr Gly			
	580	585	590
Ile Leu Thr Phe Leu Asp Ala Val Ser Trp Gly Arg Phe Ala Glu Phe			
	595	600	605
Gly Ile Trp Trp Gln Thr Gly Ser Gly Cys Lys Val Ala Gly Phe Leu			
	610	615	620
Ala Val Phe Ser Ser Glu Ser Ala Ile Phe Leu Leu Met Leu Ala Thr			
	625	630	635
Val Glu Arg Ser Leu Ser Ala Lys Asp Ile Met Lys Asn Gly Lys Ser			
	645	650	655
Asn His Leu Lys Gln Phe Arg Val Ala Ala Leu Leu Ala Phe Leu Gly			
	660	665	670
Ala Thr Val Ala Gly Cys Phe Pro Leu Phe His Arg Gly Glu Tyr Ser			
	675	680	685
Ala Ser Pro Leu Cys Leu Pro Phe Pro Thr Gly Glu Thr Pro Ser Leu			
	690	695	700
Gly Phe Thr Val Thr Leu Val Leu Leu Asn Ser Leu Ala Phe Leu Leu			
	705	710	715
Met Ala Val Ile Tyr Thr Lys Leu Tyr Cys Asn Leu Glu Lys Glu Asp			
	725	730	735
Leu Ser Glu Asn Ser Gln Ser Ser Met Ile Lys His Val Ala Trp Leu			
	740	745	750
Ile Phe Thr Asn Cys Ile Phe Phe Cys Pro Val Ala Phe Phe Ser Phe			
	755	760	765
Ala Pro Leu Ile Thr Ala Ile Ser Ile Ser Pro Glu Ile Met Lys Ser			
	770	775	780

346/518

Val Thr Leu Ile Phe Phe Pro Leu Pro Ala Cys Leu Asn Pro Val Leu  
 785                      790                      795                      800  
 Tyr Val Phe Phe Asn Pro Lys Phe Lys Glu Asp Trp Lys Leu Leu Lys  
                          805                      810                      815  
 Arg Arg Val Thr Lys Lys Ser Gly Ser Val Ser Val Ser Ile Ser Ser  
                          820                      825                      830  
 Gln Gly Gly Cys Leu Glu Gln Asp Phe Tyr Tyr Asp Cys Gly Met Tyr  
                          835                      840                      845  
 Ser His Leu Gln Gly Asn Leu Thr Val Cys Asp Cys Cys Glu Ser Phe  
                          850                      855                      860  
 Leu Leu Thr Lys Pro Val Ser Cys Lys His Leu Ile Lys Ser His Ser  
 865                      870                      875                      880  
 Cys Pro Ala Leu Ala Val Ala Ser Cys Gln Arg Pro Glu Gly Tyr Trp  
                          885                      890                      895  
 Ser Asp Cys Gly Thr Gln Ser Ala His Ser Asp Tyr Ala Asp Glu Glu  
                          900                      905                      910  
 Asp Ser Phe Val Ser Asp Ser Ser Asp Gln Val Gln Ala Cys Gly Arg  
                          915                      920                      925  
 Ala Cys Phe Tyr Gln Ser Arg Gly Phe Pro Leu Val Arg Tyr Ala Tyr  
                          930                      935                      940  
 Asn Leu Pro Arg Val Lys Asp Thr Ser Lys Gly Glu Glu Leu Phe Thr  
 945                      950                      955                      960  
 Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His  
                          965                      970                      975  
 Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys  
                          980                      985                      990  
 Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp  
                          995                      1000                      1005  
 Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg

347/518

1010                      1015                      1020  
 Tyr Pro Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro  
 1025                      1030                      1035                      1040  
 Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn  
                          1045                      1050                      1055  
 Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn  
                          1060                      1065                      1070  
 Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu  
                          1075                      1080                      1085  
 Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met  
                          1090                      1095                      1100  
 Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His  
 1105                      1110                      1115                      1120  
 Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn  
                          1125                      1130                      1135  
 Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu  
                          1140                      1145                      1150  
 Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His  
                          1155                      1160                      1165  
 Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met  
                          1170                      1175                      1180  
 Asp Glu Leu Tyr Asn  
 1185

&lt;210&gt; 127

&lt;211&gt; 586

&lt;212&gt; PRT

&lt;213&gt; Human



348/518

&lt;400&gt; 127

Met Val Asn Asn Phe Ser Gln Ala Glu Ala Val Glu Leu Cys Tyr Lys

5

10

15

Asn Val Asn Glu Ser Cys Ile Lys Thr Pro Tyr Ser Pro Gly Pro Arg

20

25

30

Ser Ile Leu Tyr Ala Val Leu Gly Phe Gly Ala Val Leu Ala Ala Phe

35

40

45

Gly Asn Leu Leu Val Met Ile Ala Ile Leu His Phe Lys Gln Leu His

50

55

60

Thr Pro Thr Asn Phe Leu Ile Ala Ser Leu Ala Cys Ala Asp Phe Leu

65

70

75

80

Val Gly Val Thr Val Met Pro Phe Ser Thr Val Arg Ser Val Glu Ser

85

90

95

Cys Trp Tyr Phe Gly Asp Ser Tyr Cys Lys Phe His Thr Cys Phe Asp

100

105

110

Thr Ser Phe Cys Phe Ala Ser Leu Phe His Leu Cys Cys Ile Ser Val

115

120

125

Asp Arg Tyr Ile Ala Val Thr Asp Pro Leu Thr Tyr Pro Thr Lys Phe

130

135

140

Thr Val Ser Val Ser Gly Ile Cys Ile Val Leu Ser Trp Phe Phe Ser

145

150

155

160

Val Thr Tyr Ser Phe Ser Ile Phe Tyr Thr Gly Ala Asn Glu Glu Gly

165

170

175

Ile Glu Glu Leu Val Val Ala Leu Thr Cys Val Gly Gly Cys Gln Ala

180

185

190

Pro Leu Asn Gln Asn Trp Val Leu Leu Cys Phe Leu Leu Phe Phe Ile

195

200

205

Pro Asn Val Ala Met Val Phe Ile Tyr Ser Lys Ile Phe Leu Val Ala

210

215

220

349/518

Lys His Gln Ala Arg Lys Ile Glu Ser Thr Ala Ser Gln Ala Gln Ser  
 225                      230                      235                      240  
 Ser Ser Glu Ser Tyr Lys Glu Arg Val Ala Lys Arg Glu Arg Lys Ala  
                     245                      250                      255  
 Ala Lys Thr Leu Gly Ile Ala Met Ala Ala Phe Leu Val Ser Trp Leu  
                     260                      265                      270  
 Pro Tyr Leu Val Asp Ala Val Ile Asp Ala Tyr Met Asn Phe Ile Thr  
                     275                      280                      285  
 Pro Pro Tyr Val Tyr Glu Ile Leu Val Trp Cys Val Tyr Tyr Asn Ser  
                     290                      295                      300  
 Ala Met Asn Pro Leu Ile Tyr Ala Phe Phe Tyr Gln Trp Phe Gly Lys  
 305                      310                      315                      320  
 Ala Ile Lys Leu Ile Val Ser Gly Lys Val Leu Arg Thr Asp Ser Ser  
                     325                      330                      335  
 Thr Thr Asn Leu Phe Ser Glu Glu Val Glu Thr Asp Ala Ser Lys Gly  
                     340                      345                      350  
 Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly  
                     355                      360                      365  
 Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp  
                     370                      375                      380  
 Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys  
 385                      390                      395                      400  
 Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val  
                     405                      410                      415  
 Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe  
                     420                      425                      430  
 Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe  
                     435                      440                      445  
 Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly

350/518

450                      455                      460  
 Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu  
 465                      470                      475                      480  
 Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His  
                          485                      490                      495  
 Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn  
                          500                      505                      510  
 Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp  
                          515                      520                      525  
 His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro  
                          530                      535                      540  
 Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn  
 545                      550                      555                      560  
 Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly  
                          565                      570                      575  
 Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
                          580                      585

&lt;210&gt; 128

&lt;211&gt; 1810

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 128

Met Thr Pro Ala Cys Pro Leu Leu Leu Ser Val Ile Leu Ser Leu Arg  
                          5                      10                      15  
 Leu Ala Thr Ala Phe Asp Pro Ala Pro Ser Ala Cys Ser Ala Leu Ala  
                          20                      25                      30  
 Ser Gly Val Leu Tyr Gly Ala Phe Ser Leu Gln Asp Leu Phe Pro Thr

351/518

35	40	45			
Ile	Ala	Ser	Gly	Cys	Ser
50	55	60	Trp	Thr	Leu
Tyr	Ser	Leu	Tyr	Leu	Arg
65	70	75	80	Asn	Arg
Phe	Ala	Pro	Arg	Leu	Leu
85	90	95	Pro	Leu	Asp
Cys	Leu	Arg	Pro	Ser	Pro
100	105	110	Glu	Glu	Ala
Val	Gly	Arg	Pro	Glu	Glu
115	120	125	Ala	Glu	Ala
Leu	Cys	Ser	Gly	Ser	Gly
130	135	140	Pro	Phe	Thr
Phe	Val	Gln	Leu	Cys	Leu
145	150	155	160	Ser	Ala
Leu	Ala	Pro	Ala	Ala	Leu
165	170	175	Ala	Phe	Arg
Asn	Asn	Asn	Asn	Ser	Ser
180	185	190	Gln	Phe	Thr
Ser	Glu	Glu	Cys	Gly	Arg
195	200	205	Ala	Gly	Arg
Pro	Gly	Cys	Ser	Cys	Pro
210	215	220	Glu	Ala	Gly
Thr	Ser	Pro	Gly	Pro	Pro
225	230	235	240	Ala	His
Pro	Gly	Gly	Pro	Ala	Pro
245	250	255	Ala	Glu	Ala
Ser	Asn	Asp	Leu	Phe	Thr
260	265	270	Thr	Thr	Glu
			Met	Arg	Tyr
			Gly	Glu	Glu
			Pro	Glu	

352/518

Glu Glu Pro Lys Val Lys Thr Gln Trp Pro Arg Ser Ala Asp Glu Pro  
 275 280 285  
 Gly Leu Tyr Met Ala Gln Thr Gly Asp Pro Ala Ala Glu Glu Trp Ser  
 290 295 300  
 Pro Trp Ser Val Cys Ser Leu Thr Cys Gly Gln Gly Leu Gln Val Arg  
 305 310 315 320  
 Thr Arg Ser Cys Val Ser Ser Pro Tyr Gly Thr Leu Cys Ser Gly Pro  
 325 330 335  
 Leu Arg Glu Thr Arg Pro Cys Asn Asn Ser Ala Thr Cys Pro Val His  
 340 345 350  
 Gly Val Trp Glu Glu Trp Gly Ser Trp Ser Leu Cys Ser Arg Ser Cys  
 355 360 365  
 Gly Arg Gly Ser Arg Ser Arg Met Arg Thr Cys Val Pro Pro Gln His  
 370 375 380  
 Gly Gly Lys Ala Cys Glu Gly Pro Glu Leu Gln Thr Lys Leu Cys Ser  
 385 390 395 400  
 Met Ala Ala Cys Pro Val Glu Gly Gln Trp Leu Glu Trp Gly Pro Trp  
 405 410 415  
 Gly Pro Cys Ser Thr Ser Cys Ala Asn Gly Thr Gln Gln Arg Ser Arg  
 420 425 430  
 Lys Cys Ser Val Ala Gly Pro Ala Trp Ala Thr Cys Thr Gly Ala Leu  
 435 440 445  
 Thr Asp Thr Arg Glu Cys Ser Asn Leu Glu Cys Pro Ala Thr Asp Ser  
 450 455 460  
 Lys Trp Gly Pro Trp Asn Ala Trp Ser Leu Cys Ser Lys Thr Cys Asp  
 465 470 475 480  
 Thr Gly Trp Gln Arg Arg Phe Arg Met Cys Gln Ala Thr Gly Thr Gln  
 485 490 495  
 Gly Tyr Pro Cys Glu Gly Thr Gly Glu Glu Val Lys Pro Cys Ser Glu

353/518

500	505	510
Lys Arg Cys Pro Ala Phe His Glu Met Cys Arg Asp Glu Tyr Val Met		
515	520	525
Leu Met Thr Trp Lys Lys Ala Ala Ala Gly Glu Ile Ile Tyr Asn Lys		
530	535	540
Cys Pro Pro Asn Ala Ser Gly Ser Ala Ser Arg Arg Cys Leu Leu Ser		
545	550	555
Ala Gln Gly Val Ala Tyr Trp Gly Leu Pro Ser Phe Ala Arg Cys Ile		
565	570	575
Ser His Glu Tyr Arg Tyr Leu Tyr Leu Ser Leu Arg Glu His Leu Ala		
580	585	590
Lys Gly Gln Arg Met Leu Ala Gly Glu Gly Met Ser Gln Val Val Arg		
595	600	605
Ser Leu Gln Glu Leu Leu Ala Arg Arg Thr Tyr Tyr Ser Gly Asp Leu		
610	615	620
Leu Phe Ser Val Asp Ile Leu Arg Asn Val Thr Asp Thr Phe Lys Arg		
625	630	635
Ala Thr Tyr Val Pro Ser Ala Asp Asp Val Gln Arg Phe Phe Gln Val		
645	650	655
Val Ser Phe Met Val Asp Ala Glu Asn Lys Glu Lys Trp Asp Asp Ala		
660	665	670
Gln Gln Val Ser Pro Gly Ser Val His Leu Leu Arg Val Val Glu Asp		
675	680	685
Phe Ile His Leu Val Gly Asp Ala Leu Lys Ala Phe Gln Ser Ser Leu		
690	695	700
Ile Val Thr Asp Asn Leu Val Ile Ser Ile Gln Arg Glu Pro Val Ser		
705	710	715
Ala Val Ser Ser Asp Ile Thr Phe Pro Met Arg Gly Arg Arg Gly Met		
725	730	735

354/518

Lys Asp Trp Val Arg His Ser Glu Asp Arg Leu Phe Leu Pro Lys Glu

740

745

750

Val Leu Ser Leu Ser Ser Pro Gly Lys Pro Ala Thr Ser Gly Ala Ala

755

760

765

Gly Ser Pro Gly Arg Gly Arg Gly Pro Gly Thr Val Pro Pro Gly Pro

770

775

780

Gly His Ser His Gln Arg Leu Leu Pro Ala Asp Pro Asp Glu Ser Ser

785

790

795

800

Tyr Phe Val Ile Gly Ala Val Leu Tyr Arg Thr Leu Gly Leu Ile Leu

805

810

815

Pro Pro Pro Arg Pro Pro Leu Ala Val Thr Ser Arg Val Met Thr Val

820

825

830

Thr Val Arg Pro Pro Thr Gln Pro Pro Ala Glu Pro Leu Ile Thr Val

835

840

845

Glu Leu Ser Tyr Ile Ile Asn Gly Thr Thr Asp Pro His Cys Ala Ser

850

855

860

Trp Asp Tyr Ser Arg Ala Asp Ala Ser Ser Gly Asp Trp Asp Thr Glu

865

870

875

880

Asn Cys Gln Thr Leu Glu Thr Gln Ala Ala His Thr Arg Cys Gln Cys

885

890

895

Gln His Leu Ser Thr Phe Ala Val Leu Ala Gln Pro Pro Lys Asp Leu

900

905

910

Thr Leu Glu Leu Ala Gly Ser Pro Ser Val Pro Leu Val Ile Gly Cys

915

920

925

Ala Val Ser Cys Met Ala Leu Leu Thr Leu Leu Ala Ile Tyr Ala Ala

930

935

940

Phe Trp Arg Phe Ile Lys Ser Glu Arg Ser Ile Ile Leu Leu Asn Phe

945

950

955

960

Cys Leu Ser Ile Leu Ala Ser Asn Ile Leu Ile Leu Val Gly Gln Ser

355/518

	965	970	975
Arg Val Leu Ser Lys Gly Val Cys Thr Met Thr Ala Ala Phe Leu His			
980	985	990	
Phe Phe Phe Leu Ser Ser Phe Cys Trp Val Leu Thr Glu Ala Trp Gln			
995	1000	1005	
Ser Tyr Leu Ala Val Ile Gly Arg Met Arg Thr Arg Leu Val Arg Lys			
1010	1015	1020	
Arg Phe Leu Cys Leu Gly Trp Gly Leu Pro Ala Leu Val Val Ala Val			
1025	1030	1035	1040
Ser Val Gly Phe Thr Arg Thr Lys Gly Tyr Gly Thr Ser Ser Tyr Cys			
1045	1050	1055	
Trp Leu Ser Leu Glu Gly Gly Leu Leu Tyr Ala Phe Val Gly Pro Ala			
1060	1065	1070	
Ala Val Ile Val Leu Val Asn Met Leu Ile Gly Ile Ile Val Phe Asn			
1075	1080	1085	
Lys Leu Met Ala Arg Asp Gly Ile Ser Asp Lys Ser Lys Lys Gln Arg			
1090	1095	1100	
Ala Gly Ser Glu Arg Cys Pro Trp Ala Ser Leu Leu Leu Pro Cys Ser			
1105	1110	1115	1120
Ala Cys Gly Ala Val Pro Ser Pro Leu Leu Ser Ser Ala Ser Ala Arg			
1125	1130	1135	
Asn Ala Met Ala Ser Leu Trp Ser Ser Cys Val Val Leu Pro Leu Leu			
1140	1145	1150	
Ala Leu Thr Trp Met Ser Ala Val Leu Ala Met Thr Asp Arg Arg Ser			
1155	1160	1165	
Val Leu Phe Gln Ala Leu Phe Ala Val Phe Asn Ser Ala Gln Gly Phe			
1170	1175	1180	
Val Ile Thr Ala Val His Cys Phe Leu Arg Arg Glu Val Gln Asp Val			
1185	1190	1195	1200



356/518

Val Lys Cys Gln Met Gly Val Cys Arg Ala Asp Glu Ser Glu Asp Ser  
 1205 1210 1215  
 Pro Asp Ser Cys Lys Asn Gly Gln Leu Gln Ile Leu Ser Asp Phe Glu  
 1220 1225 1230  
 Lys Asp Val Asp Leu Ala Cys Gln Thr Val Leu Phe Lys Glu Val Asn  
 1235 1240 1245  
 Thr Cys Asn Pro Ser Thr Ile Thr Gly Thr Leu Ser Arg Leu Ser Leu  
 1250 1255 1260  
 Asp Glu Asp Glu Glu Pro Lys Ser Cys Leu Val Gly Pro Glu Gly Ser  
 1265 1270 1275 1280  
 Leu Ser Phe Ser Pro Leu Pro Gly Asn Ile Leu Val Pro Met Ala Ala  
 1285 1290 1295  
 Ser Pro Gly Leu Gly Glu Pro Pro Pro Pro Gln Glu Ala Asn Pro Val  
 1300 1305 1310  
 Tyr Met Cys Gly Glu Gly Gly Leu Arg Gln Leu Asp Leu Thr Trp Leu  
 1315 1320 1325  
 Arg Pro Thr Glu Pro Gly Ser Glu Gly Asp Tyr Met Val Leu Pro Arg  
 1330 1335 1340  
 Arg Thr Leu Ser Leu Gln Pro Gly Gly Gly Gly Gly Gly Glu Asp  
 1345 1350 1355 1360  
 Ala Pro Arg Ala Arg Pro Glu Gly Thr Pro Arg Arg Ala Ala Lys Thr  
 1365 1370 1375  
 Val Ala His Thr Glu Gly Tyr Pro Ser Phe Leu Ser Val Asp His Ser  
 1380 1385 1390  
 Gly Leu Gly Leu Gly Pro Ala Tyr Gly Ser Leu Gln Asn Pro Tyr Gly  
 1395 1400 1405  
 Met Thr Phe Gln Pro Pro Pro Pro Thr Pro Ser Ala Arg Gln Val Pro  
 1410 1415 1420  
 Glu Pro Gly Glu Arg Ser Arg Thr Met Pro Arg Thr Val Pro Gly Ser

357/518

1425	1430	1435	1440
Thr Met Lys Met Gly Ser Leu Glu Arg Lys Lys Leu Arg Tyr Ser Asp			
	1445	1450	1455
Leu Asp Phe Glu Val Met His Thr Arg Lys Arg His Ser Glu Leu Tyr			
	1460	1465	1470
His Glu Leu Asn Gln Lys Phe His Thr Phe Asp Arg Tyr Arg Ser Gln			
	1475	1480	1485
Ser Thr Ala Lys Arg Glu Lys Arg Trp Ser Val Ser Ser Gly Gly Ala			
	1490	1495	1500
Ala Glu Arg Ser Val Cys Thr Asp Lys Pro Ser Pro Gly Glu Arg Pro			
1505	1510	1515	1520
Ser Leu Ser Gln His Arg Arg His Gln Ser Trp Ser Thr Phe Lys Ser			
	1525	1530	1535
Met Thr Leu Gly Ser Leu Pro Pro Lys Pro Arg Glu Arg Leu Thr Leu			
	1540	1545	1550
His Arg Ala Ala Ala Trp Glu Pro Thr Glu Pro Pro Asp Gly Asp Phe			
	1555	1560	1565
Gln Thr Glu Val Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val			
	1570	1575	1580
Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser			
1585	1590	1595	1600
Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu			
	1605	1610	1615
Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu			
	1620	1625	1630
Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp			
	1635	1640	1645
His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr			
	1650	1655	1660

358/518

Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr  
 1665                      1670                      1675                      1680  
 Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu  
                          1685                      1690                      1695  
 Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys  
                          1700                      1705                      1710  
 Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys  
                          1715                      1720                      1725  
 Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile Glu  
                          1730                      1735                      1740  
 Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile  
 1745                      1750                      1755                      1760  
 Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln  
                          1765                      1770                      1775  
 Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu  
                          1780                      1785                      1790  
 Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu Leu  
                          1795                      1800                      1805  
 Tyr Asn  
 1810

&lt;210&gt; 129

&lt;211&gt; 563

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 129

Met Asp Gly Ser Asn Val Thr Ser Phe Val Val Glu Glu Pro Thr Asn

5

10

15

359/518

Ile Ser Thr Gly Arg Asn Ala Ser Val Gly Asn Ala His Arg Gln Ile  
                   20                  25                  30  
 Pro Ile Val His Trp Val Ile Met Ser Ile Ser Pro Val Gly Phe Val  
                   35                  40                  45  
 Glu Asn Gly Ile Leu Leu Trp Phe Leu Cys Phe Arg Met Arg Arg Asn  
                   50                  55                  60  
 Pro Phe Thr Val Tyr Ile Thr His Leu Ser Ile Ala Asp Ile Ser Leu  
                   65                  70                  75                  80  
 Leu Phe Cys Ile Phe Ile Leu Ser Ile Asp Tyr Ala Leu Asp Tyr Glu  
                                   85                  90                  95  
 Leu Ser Ser Gly His Tyr Tyr Thr Ile Val Thr Leu Ser Val Thr Phe  
                   100                  105                  110  
 Leu Phe Gly Tyr Asn Thr Gly Leu Tyr Leu Leu Thr Ala Ile Ser Val  
                   115                  120                  125  
 Glu Arg Cys Leu Ser Val Leu Tyr Pro Ile Trp Tyr Arg Cys His Arg  
                   130                  135                  140  
 Pro Lys Tyr Gln Ser Ala Leu Val Cys Ala Leu Leu Trp Ala Leu Ser  
                   145                  150                  155                  160  
 Cys Leu Val Thr Thr Met Glu Tyr Val Met Cys Ile Asp Arg Glu Glu  
                   165                  170                  175  
 Glu Ser His Ser Arg Asn Asp Cys Arg Ala Val Ile Ile Phe Ile Ala  
                   180                  185                  190  
 Ile Leu Ser Phe Leu Val Phe Thr Pro Leu Met Leu Val Ser Ser Thr  
                   195                  200                  205  
 Ile Leu Val Val Lys Ile Arg Lys Asn Thr Trp Ala Ser His Ser Ser  
                   210                  215                  220  
 Lys Leu Tyr Ile Val Ile Met Val Thr Ile Ile Ile Phe Leu Ile Phe  
                   225                  230                  235                  240  
 Ala Met Pro Met Arg Leu Leu Tyr Leu Leu Tyr Tyr Glu Tyr Trp Ser

360/518

	245	250	255
Thr Phe Gly Asn Leu His His Ile Ser Leu Leu Phe Ser Thr Ile Asn			
	260	265	270
Ser Ser Ala Asn Pro Phe Ile Tyr Phe Phe Val Gly Ser Ser Lys Lys			
	275	280	285
Lys Arg Phe Lys Glu Ser Leu Lys Val Val Leu Thr Arg Ala Phe Lys			
	290	295	300
Asp Glu Met Gln Pro Arg Arg Gln Lys Asp Asn Cys Asn Thr Val Thr			
305	310	315	320
Val Glu Thr Val Val Ala Ser Lys Gly Glu Glu Leu Phe Thr Gly Val			
	325	330	335
Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe			
	340	345	350
Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr			
	355	360	365
Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr			
	370	375	380
Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro			
385	390	395	400
Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly			
	405	410	415
Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys			
	420	425	430
Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile			
	435	440	445
Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His			
	450	455	460
Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp			
465	470	475	480

361/518

Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile  
                     485                    490                    495  
 Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro  
                     500                    505                    510  
 Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr  
                     515                    520                    525  
 Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val  
                     530                    535                    540  
 Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu  
 545                    550                    555                    560  
 Leu Tyr Asn

&lt;210&gt; 130

&lt;211&gt; 707

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 130

Met Gln Met Ala Asp Ala Ala Thr Ile Ala Thr Met Asn Lys Ala Ala  
                     5                    10                    15  
 Gly Gly Asp Lys Leu Ala Glu Leu Phe Ser Leu Val Pro Asp Leu Leu  
                     20                    25                    30  
 Glu Ala Ala Asn Thr Ser Gly Asn Ala Ser Leu Gln Leu Pro Asp Leu  
                     35                    40                    45  
 Trp Trp Glu Leu Gly Leu Glu Leu Pro Asp Gly Ala Pro Pro Gly His  
                     50                    55                    60  
 Pro Pro Gly Ser Gly Gly Ala Glu Ser Ala Asp Thr Glu Ala Arg Val  
                     65                    70                    75                    80  
 Arg Ile Leu Ile Ser Val Val Tyr Trp Val Val Cys Ala Leu Gly Leu

362/518

85	90	95
Ala Gly Asn Leu Leu Val Leu Tyr Leu Met Lys Ser Met Gln Gly Trp		
100	105	110
Arg Lys Ser Ser Ile Asn Leu Phe Val Thr Asn Leu Ala Leu Thr Asp		
115	120	125
Phe Gln Phe Val Leu Thr Leu Pro Phe Trp Ala Val Glu Asn Ala Leu		
130	135	140
Asp Phe Lys Trp Pro Phe Gly Lys Ala Met Cys Lys Ile Val Ser Met		
145	150	155
Val Thr Ser Met Asn Met Tyr Ala Ser Val Phe Phe Leu Thr Ala Met		
165	170	175
Ser Val Thr Arg Tyr His Ser Val Ala Ser Ala Leu Lys Ser His Arg		
180	185	190
Thr Arg Gly His Gly Arg Gly Asp Cys Cys Gly Arg Ser Leu Gly Asp		
195	200	205
Ser Cys Cys Phe Ser Ala Lys Ala Leu Cys Val Trp Ile Trp Ala Leu		
210	215	220
Ala Ala Leu Ala Ser Leu Pro Ser Ala Ile Phe Ser Thr Thr Val Lys		
225	230	235
Val Met Gly Glu Glu Leu Cys Leu Val Arg Phe Pro Asp Lys Leu Leu		
245	250	255
Gly Arg Asp Arg Gln Phe Trp Leu Gly Leu Tyr His Ser Gln Lys Val		
260	265	270
Leu Leu Gly Phe Val Leu Pro Leu Gly Ile Ile Ile Leu Cys Tyr Leu		
275	280	285
Leu Leu Val Arg Phe Ile Ala Asp Arg Arg Ala Ala Gly Thr Lys Gly		
290	295	300
Gly Ala Ala Val Ala Gly Gly Arg Pro Thr Gly Ala Ser Ala Arg Arg		
305	310	315
		320

363/518

Leu Ser Lys Val Thr Lys Ser Val Thr Ile Val Val Leu Ser Phe Phe  
 325 330 335  
 Leu Cys Trp Leu Pro Asn Gln Ala Leu Thr Thr Trp Ser Ile Leu Ile  
 340 345 350  
 Lys Phe Asn Ala Val Pro Phe Ser Gln Glu Tyr Phe Leu Cys Gln Val  
 355 360 365  
 Tyr Ala Phe Pro Val Ser Val Cys Leu Ala His Ser Asn Ser Cys Leu  
 370 375 380  
 Asn Pro Val Leu Tyr Cys Leu Val Arg Arg Glu Phe Arg Lys Ala Leu  
 385 390 395 400  
 Lys Ser Leu Leu Trp Arg Ile Ala Ser Pro Ser Ile Thr Ser Met Arg  
 405 410 415  
 Pro Phe Thr Ala Thr Thr Lys Pro Glu His Glu Asp Gln Gly Leu Gln  
 420 425 430  
 Ala Pro Ala Pro Pro His Ala Ala Ala Glu Pro Asp Leu Leu Tyr Tyr  
 435 440 445  
 Pro Pro Gly Val Val Val Tyr Ser Gly Gly Arg Tyr Asp Leu Leu Pro  
 450 455 460  
 Ser Ser Ser Ala Tyr Thr Ser Lys Gly Glu Glu Leu Phe Thr Gly Val  
 465 470 475 480  
 Val Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe  
 485 490 495  
 Ser Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr  
 500 505 510  
 Leu Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr  
 515 520 525  
 Leu Val Thr Thr Leu Cys Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro  
 530 535 540  
 Asp His Met Lys Arg His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly



364/518

545                      550                      555                      560  
 Tyr Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys  
                          565                      570                      575  
 Thr Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile  
                          580                      585                      590  
 Glu Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His  
                          595                      600                      605  
 Lys Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp  
                          610                      615                      620  
 Lys Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Thr Arg His Asn Ile  
 625                      630                      635                      640  
 Glu Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro  
                          645                      650                      655  
 Ile Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr  
                          660                      665                      670  
 Gln Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val  
                          675                      680                      685  
 Leu Leu Glu Phe Val Thr Ala Ala Gly Ile Thr His Gly Met Asp Glu  
                          690                      695                      700  
 Leu Tyr Asn  
 705

&lt;210&gt; 131

&lt;211&gt; 746

&lt;212&gt; PRT

&lt;213&gt; Human

&lt;400&gt; 131

Met Thr Ser Thr Cys Thr Asn Ser Thr Arg Glu Ser Asn Ser Ser His

365/518

	5	10	15
Thr Cys Met Pro Leu Ser Lys Met Pro Ile Ser Leu Ala His Gly Ile			
	20	25	30
Ile Arg Ser Thr Val Leu Val Ile Phe Leu Ala Ala Ser Phe Val Gly			
	35	40	45
Asn Ile Val Leu Ala Leu Val Leu Gln Arg Lys Pro Gln Leu Leu Gln			
	50	55	60
Val Thr Asn Arg Phe Ile Phe Asn Leu Leu Val Thr Asp Leu Leu Gln			
	65	70	75
Ile Ser Leu Val Ala Pro Trp Val Val Ala Thr Ser Val Pro Leu Phe			
	85	90	95
Trp Pro Leu Asn Ser His Phe Cys Thr Ala Leu Val Ser Leu Thr His			
	100	105	110
Leu Phe Ala Phe Ala Ser Val Asn Thr Ile Val Leu Val Ser Val Asp			
	115	120	125
Arg Tyr Leu Ser Ile Ile His Pro Leu Ser Tyr Pro Ser Lys Met Thr			
	130	135	140
Gln Arg Arg Gly Tyr Leu Leu Leu Tyr Gly Thr Trp Ile Val Ala Ile			
	145	150	155
Leu Gln Ser Thr Pro Pro Leu Tyr Gly Trp Gly Gln Ala Ala Phe Asp			
	165	170	175
Glu Arg Asn Ala Leu Cys Ser Met Ile Trp Gly Ala Ser Pro Ser Tyr			
	180	185	190
Thr Ile Leu Ser Val Val Ser Phe Ile Val Ile Pro Leu Ile Val Met			
	195	200	205
Ile Ala Cys Tyr Ser Val Val Phe Cys Ala Ala Arg Arg Gln His Ala			
	210	215	220
Leu Leu Tyr Asn Val Lys Arg His Ser Leu Glu Val Arg Val Lys Asp			
	225	230	235
			240

366/518

Cys Val Glu Asn Glu Asp Glu Glu Gly Ala Glu Lys Lys Glu Glu Phe  
                   245                  250                  255  
 Gln Asp Glu Ser Glu Phe Arg Arg Gln His Glu Gly Glu Val Lys Ala  
                   260                  265                  270  
 Lys Glu Gly Arg Met Glu Ala Lys Asp Gly Ser Leu Lys Ala Lys Glu  
                   275                  280                  285  
 Gly Ser Thr Gly Thr Ser Glu Ser Ser Val Glu Ala Arg Gly Ser Glu  
                   290                  295                  300  
 Glu Val Arg Glu Ser Ser Thr Val Ala Ser Asp Gly Ser Met Glu Gly  
 305                  310                  315                  320  
 Lys Glu Gly Ser Thr Lys Val Glu Glu Asn Ser Met Lys Ala Asp Lys  
                   325                  330                  335  
 Gly Arg Thr Glu Val Asn Gln Cys Ser Ile Asp Leu Gly Glu Asp Asp  
                   340                  345                  350  
 Met Glu Phe Gly Glu Asp Asp Ile Asn Phe Ser Glu Asp Asp Val Glu  
                   355                  360                  365  
 Ala Val Asn Ile Pro Glu Ser Leu Pro Pro Ser Arg Arg Asn Ser Asn  
                   370                  375                  380  
 Ser Asn Pro Pro Leu Pro Arg Cys Tyr Gln Cys Lys Ala Ala Lys Val  
 385                  390                  395                  400  
 Ile Phe Ile Ile Ile Phe Ser Tyr Val Leu Ser Leu Gly Pro Tyr Cys  
                   405                  410                  415  
 Phe Leu Ala Val Leu Ala Val Trp Val Asp Val Glu Thr Gln Val Pro  
                   420                  425                  430  
 Gln Trp Val Ile Thr Ile Ile Ile Trp Leu Phe Phe Leu Gln Cys Cys  
                   435                  440                  445  
 Ile His Pro Tyr Val Tyr Gly Tyr Met His Lys Thr Ile Lys Lys Glu  
                   450                  455                  460  
 Ile Gln Asp Met Leu Lys Lys Phe Phe Cys Lys Glu Lys Pro Pro Lys

367/518

465	470	475	480
Glu Asp Ser His Pro Asp Leu Pro Gly Thr Glu Gly Gly Thr Glu Gly			
	485	490	495
Lys Ile Val Pro Ser Tyr Asp Ser Ala Thr Phe Pro Ala Ser Lys Gly			
	500	505	510
Glu Glu Leu Phe Thr Gly Val Val Pro Ile Leu Val Glu Leu Asp Gly			
	515	520	525
Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp			
	530	535	540
Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys			
	545	550	555
Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr Leu Cys Tyr Gly Val			
	565	570	575
Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys Arg His Asp Phe Phe			
	580	585	590
Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu Arg Thr Ile Phe Phe			
	595	600	605
Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu Val Lys Phe Glu Gly			
	610	615	620
Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly Ile Asp Phe Lys Glu			
	625	630	635
Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr Asn Tyr Asn Ser His			
	645	650	655
Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn Gly Ile Lys Val Asn			
	660	665	670
Phe Lys Thr Arg His Asn Ile Glu Asp Gly Ser Val Gln Leu Ala Asp			
	675	680	685
His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly Pro Val Leu Leu Pro			
	690	695	700

368/518

Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu Ser Lys Asp Pro Asn  
 705                      710                      715                      720  
 Glu Lys Arg Asp His Met Val Leu Leu Glu Phe Val Thr Ala Ala Gly  
                          725                      730                      735  
 Ile Thr His Gly Met Asp Glu Leu Tyr Asn  
                          740                      745

&lt;210&gt; 132

&lt;211&gt; 1635

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 132

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atgtattcat ttatggcagg atccatattc atcacaatat ttggcaatct tgccatgata   60
atttccattt cctacttcaa gcagttcac  acaccaacca acttccatcat cctctccatg  120
gccatcactg atttccctct gggattcacc atcatgccat atagtatgat cagatcggtg   180
gagaactgct ggtattttgg gcttacattt tgcaagattt attatagttt tgacctgatg   240
cttagcataa catccatttt tcattcttgc tcagtggcca ttgatagatt ttatgctata   300
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&lt;211&gt; 1839

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 133

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&lt;210&gt; 134

&lt;211&gt; 1800

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 134

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&lt;210&gt; 135

&lt;211&gt; 2673

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 135

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&lt;211&gt; 1797

&lt;212&gt; DNA

&lt;213&gt; Human

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&lt;400&gt; 136

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&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 137

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&lt;211&gt; 1926

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 138

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&lt;210&gt; 139

&lt;211&gt; 1746

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 139

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378/518

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379/518

&lt;211&gt; 3759

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 140

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380/518

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&lt;210&gt; 141

&lt;211&gt; 1968

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 141

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&lt;210&gt; 142

&lt;211&gt; 1722

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 142

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383/518

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&lt;210&gt; 143

&lt;211&gt; 2763

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 143

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385/518

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&lt;210&gt; 144

&lt;211&gt; 2301

&lt;212&gt; DNA

&lt;213&gt; Human

386/518

&lt;400&gt; 144

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&lt;210&gt; 145

&lt;211&gt; 3375

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 145

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&lt;210&gt; 146

&lt;211&gt; 1800

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 146

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&lt;211&gt; 1674

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&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 147

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&lt;210&gt; 148

&lt;211&gt; 2127

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 148

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&lt;210&gt; 149

&lt;211&gt; 1914

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 149

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&lt;210&gt; 150

395/518

&lt;211&gt; 1974

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 150

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&lt;210&gt; 151

&lt;211&gt; 1836

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 151

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&lt;210&gt; 152

&lt;211&gt; 2397

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 152

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&lt;210&gt; 153

&lt;211&gt; 1674

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 153

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&lt;210&gt; 154

&lt;211&gt; 1791

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 154

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&lt;210&gt; 155

&lt;211&gt; 1719

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 155

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402/518

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&lt;210&gt; 156

&lt;211&gt; 1728

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 156

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&lt;210&gt; 157

&lt;211&gt; 1743

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 157

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&lt;211&gt; 1752

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 158

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&lt;211&gt; 2556

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 159

407/518

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&lt;211&gt; 2688

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 160

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&lt;211&gt; 3447

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 161

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&lt;210&gt; 162

&lt;211&gt; 1929

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 162

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gacaaccatt acctgtccac acaatctgcc ctctcgaaag atcccaacga aaagagagac 1860
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tacaactga 1929

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&lt;210&gt; 163

&lt;211&gt; 1962

414/518

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 163

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415/518

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&lt;210&gt; 164

&lt;211&gt; 1833

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 164

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416/518

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&lt;210&gt; 165

&lt;211&gt; 1752

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 165

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cccacccagc tcctcttctt cctgagtgtc ctggggtctt tcggactcgc ttttgcttc 240
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417/518

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&lt;210&gt; 166

&lt;211&gt; 3618

&lt;212&gt; DNA

418/518

&lt;213&gt; Human

&lt;400&gt; 166

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419/518

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420/518

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&lt;210&gt; 167

&lt;211&gt; 1722

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 167

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421/518

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&lt;210&gt; 168

&lt;211&gt; 1839

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 168

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422/518

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&lt;210&gt; 169

&lt;211&gt; 1836

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 169

423/518

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&lt;210&gt; 170

&lt;211&gt; 2016

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 170

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&lt;210&gt; 171

&lt;211&gt; 1800

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 171

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&lt;210&gt; 172

&lt;211&gt; 1728

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 172

427/518

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&lt;210&gt; 173

&lt;211&gt; 2184

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 173

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429/518

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&lt;210&gt; 174

&lt;211&gt; 1851

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 174

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&lt;210&gt; 175

&lt;211&gt; 1827

&lt;212&gt; DNA

&lt;213&gt; Human

431/518

&lt;400&gt; 175

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432/518

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&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 176

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433/518

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&lt;210&gt; 177

&lt;211&gt; 1842

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 177

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434/518

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&lt;210&gt; 178

&lt;211&gt; 1725

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 178

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435/518

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436/518

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&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 179

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437/518

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438/518

aactga

3186

&lt;210&gt; 180

&lt;211&gt; 2262

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 180

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439/518

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&lt;210&gt; 181

&lt;211&gt; 1803

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 181

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440/518

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&lt;210&gt; 182

&lt;211&gt; 2019

441/518

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 182

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&lt;210&gt; 183

&lt;211&gt; 1629

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 183

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443/518

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tacaactga 1629

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&lt;210&gt; 184

&lt;211&gt; 1716

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 184

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&lt;210&gt; 185

&lt;211&gt; 1734

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;220&gt;

445/518

&lt;221&gt;

&lt;222&gt; 330

&lt;223&gt; n stands for any base

&lt;400&gt; 185

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&lt;210&gt; 186

&lt;211&gt; 1644

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 186

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 aacctggcgg tggccgacct ctgcctgctg tgcaccttgc ccttcgtgct gcactccctg 240  
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&lt;210&gt; 187

&lt;211&gt; 2040

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 187

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&lt;210&gt; 188

&lt;211&gt; 1878

&lt;212&gt; DNA

&lt;213&gt; Human

449/518

&lt;400&gt; 188

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&lt;210&gt; 189

&lt;211&gt; 2337

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 189

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451/518

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&lt;210&gt; 190

&lt;211&gt; 1755

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 190

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&lt;210&gt; 191

&lt;211&gt; 1758

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 191

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454/518

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&lt;210&gt; 192

&lt;211&gt; 1836

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 192

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455/518

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&lt;210&gt; 193

&lt;211&gt; 1776

&lt;212&gt; DNA

&lt;213&gt; Rat

&lt;400&gt; 193

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456/518

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&lt;210&gt; 194

&lt;211&gt; 1707

&lt;212&gt; DNA

457/518

&lt;213&gt; Human

&lt;400&gt; 194

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458/518

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&lt;210&gt; 195

&lt;211&gt; 1803

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 195

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&lt;210&gt; 196

&lt;211&gt; 1788

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 196

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&lt;400&gt; 198

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466/518

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&lt;211&gt; 1707

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 207

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&lt;210&gt; 208

&lt;211&gt; 1653

&lt;212&gt; DNA

&lt;213&gt; Human.

&lt;400&gt; 208

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&lt;210&gt; 209

&lt;211&gt; 1686

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 209

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481/518

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&lt;210&gt; 210

&lt;211&gt; 1776

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&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 210

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&lt;210&gt; 211

&lt;211&gt; 1791

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 211

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&lt;210&gt; 212

&lt;211&gt; 1632

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 212

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&lt;210&gt; 213

&lt;211&gt; 1734

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 213

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487/518

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 214

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488/518

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&lt;211&gt; 2364

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 215

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489/518

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&lt;211&gt; 1827

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 216

490/518

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491/518

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&lt;211&gt; 1734

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 217

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&lt;211&gt; 2556

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&lt;213&gt; Human

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2556

&lt;210&gt; 219

&lt;211&gt; 2160

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 219

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&lt;211&gt; 1776

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 220

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496/518

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&lt;211&gt; 1785

&lt;212&gt; DNA

&lt;213&gt; Human

497/518

&lt;400&gt; 221

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&lt;211&gt; 4380

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 222

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&lt;210&gt; 223

&lt;211&gt; 1914

&lt;212&gt; DNA

&lt;213&gt; Human

501/518

&lt;400&gt; 223

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&lt;211&gt; 2076

&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 224

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&lt;210&gt; 225

&lt;211&gt; 1986

&lt;212&gt; DNA

&lt;213&gt; Human.

&lt;400&gt; 225

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1986

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&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 226

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&lt;212&gt; DNA

&lt;213&gt; Human

&lt;400&gt; 227

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&lt;213&gt; Human

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514/518

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515/518

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516/518

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517/518

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518/518

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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP03/01901

A. CLASSIFICATION OF SUBJECT MATTER  
Int.Cl<sup>7</sup> G01N33/50, G01N33/15, C12N15/09

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
Int.Cl<sup>7</sup> G01N33/50, G01N33/15, C12N15/09

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
Jitsuyo Shinan Koho 1922-1996 Toroku Jitsuyo Shinan Koho 1994-2003  
Kokai Jitsuyo Shinan Koho 1971-2003 Jitsuyo Shinan Toroku Koho 1996-2003

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00/49416 A (UNIVERSITY COURT OF THE UNIVERSITY OF GLASGOW),	1-6, 11, 12, 22-28
Y	24 August, 2000 (24.08.00), & AU 200026797 A & NO 200103997 A & CN 1372642 A & JP 2002-541439 A	7-10, 13-21
Y	Mercuty™ Pathway Profiling System User Manual, CLONTECH, 02 March, 2001 (02.03.01), pages 1 to 27	7-10, 13-21
Y	Bo-yeon KIM, Involvement of SH2-SH2-SH3 domain of phospholipase Cyl in NF-κB signaling, FEBS Letters, vol.472, pages 45 to 49, 2000	7-10, 13-21

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document but published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search  
23 April, 2003 (23.04.03)

Date of mailing of the international search report  
13 May, 2003 (13.05.03)

Name and mailing address of the ISA/  
Japanese Patent Office

Authorized officer

Facsimile No.

Telephone No.

## A. 発明の属する分野の分類 (国際特許分類 (IPC))

Int. Cl.<sup>7</sup> G01N 33/50 G01N 33/15 C12N 15/09

## B. 調査を行った分野

調査を行った最小限資料 (国際特許分類 (IPC))

Int. Cl.<sup>7</sup> G01N 33/50 G01N 33/15 C12N 15/09

最小限資料以外の資料で調査を行った分野に含まれるもの

日本国実用新案公報 1922-1996年  
 日本国公開実用新案公報 1971-2003年  
 日本国登録実用新案公報 1994-2003年  
 日本国実用新案登録公報 1996-2003年

国際調査で使用した電子データベース (データベースの名称、調査に使用した用語)

## C. 関連すると認められる文献

引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号
X	WO 00/49416 A (UNIVERSITY COURT OF THE UNIVERSITY OF GLASGOW) 2000.08.24	1-6, 11, 12, 22-28
Y	& AU 200026797 A & NO 200103997 A & CN 1372642 A & JP 2002-541439 A	7-10, 13-21
Y	Mercuty™ Pathway Profiling System User Manual, CLONTECH, 2001.03.02, p.1-27	7-10, 13-21

☒ C欄の続きにも文献が列挙されている。☐ パテントファミリーに関する別紙を参照。

## \* 引用文献のカテゴリー

「A」 特に関連のある文献ではなく、一般的技術水準を示すもの  
 「E」 国際出願日前の出願または特許であるが、国際出願日以後に公表されたもの  
 「L」 優先権主張に疑義を提起する文献又は他の文献の発行日若しくは他の特別な理由を確立するために引用する文献 (理由を付す)  
 「O」 口頭による開示、使用、展示等に言及する文献  
 「P」 国際出願日前で、かつ優先権の主張の基礎となる出願

の日の後に公表された文献  
 「T」 国際出願日又は優先日後に公表された文献であって出願と矛盾するものではなく、発明の原理又は理論の理解のために引用するもの  
 「X」 特に関連のある文献であって、当該文献のみで発明の新規性又は進歩性がないと考えられるもの  
 「Y」 特に関連のある文献であって、当該文献と他の1以上の文献との、当業者にとって自明である組合せによって進歩性がないと考えられるもの  
 「&」 同一パテントファミリー文献

国際調査を完了した日

23.04.03

国際調査報告の発送日

13.05.03

国際調査機関の名称及びあて先

日本国特許庁 (ISA/JP)  
 郵便番号100-8915  
 東京都千代田区霞が関三丁目4番3号

特許庁審査官 (権限のある職員)

宮澤 浩



2J 9407

電話番号 03-3581-1101 内線 3251

C (続き) . 関連すると認められる文献		
引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号
Y	Bo-yeon KIM, Involvement of SH2-SH2-SH3 domain of phospholipase C $\gamma$ 1 in NF- $\kappa$ B signaling, FEBS Letters, vol. 472, p. 45-49, 2000	7-10, 13-21

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